



# SURGERY

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and Science of Surgery

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# SURGERY

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## Original Communications

### *Symposium on Tumors of the Hands and Feet*

#### SYMPOSIUM: TUMORS OF THE HANDS AND FEET

##### INTRODUCTION

GEORGE T. PACK, M.D., NEW YORK, N. Y.  
(From the Memorial Hospital for Cancer and Allied Diseases.)

##### GENERAL CONSIDERATIONS

**E**ARLY Diagnosis.—Perhaps no regions or organs in the body are so readily favored for the early detection of tumors as are the hands and feet. Constantly under inspection, always sensitive to pain, irritation, swelling, and impairment of function, it would seem that no tumor could grow for long without early detection by the patient. Such extreme end results as the mutilation or amputation of an extremity or ultimate loss of life are the results not only of the inherent tendencies of some of these malignant tumors but more important still are often due to two avoidable losses of time. The culpability for failure to treat early tumors of the hands and feet falls either on the patient or first physician consulted, depending respectively on the time elapsing between the first recognized appearance of the tumor and the first visit to a physician, and the second period occurring between the first medical consultation and the institution of proper treatment.

*Multicentric Origin.*—Surgeons and pathologists are cognizant of the origin of some tumors, usually benign, in multiple foci of origin in the same organ; e.g., leiomyomas of uterus, gastrointestinal polyposis, generalized neurofibromatosis, intraductal and intraeystic papillomas, and papillary carcinomas of the breast. This tendency is decidedly not common for the various regional locations of neoplasms, excluding the hands and feet, where it seems to be the rule rather than the exception. The explanation of this multicentricity is difficult to analyze because so many factors are involved. The congenital origin of some

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of these tumors seems established; for instance, multiple enchondromas, endothelial myeloma, pigmented naevi, and melanomas. In other cases a precancerosis, common to both hands, exists which later changes to multiple epitheliomas. Epitheliomas of the dorsum of the hands are often multiple and bilateral; they may appear simultaneously or at different times if the underlying precancerous state is permitted to exist or is not constantly observed. Xanthomas or giant cell tumors of tendon sheath may be single or multiple; the basic cause here may be inflammatory, as there is histologic evidence suggesting that the process merges from an inflammatory to a neoplastic hyperplasia. The idiopathic multiple hemorrhagic sarcoma of Kaposi develops bilaterally and usually concurrently on the feet and ankles of Slavie and Southern European males, who have a common physical habitus; namely, flat-feet, short sturdy legs, thick ankles, tight inelastic skin, and coexistent or antecedent circulatory disturbances of the lower extremities, such as varicosities and edema. It is inconceivable that the Kaposi tumor on one foot is a crossed metastasis from the tumor of the opposite foot, as in the beginning there is no evidence of intervening disease. Hence in Kaposi's disease there is the classical example of malignant tumors occurring multicentrically and in similar tissues, yet at such distances from each other as to defy any explanation other than the existence of a common predisposing state. At the onset the first lesions may resemble infection, but this is probably not the true mode of genesis for two reasons. Our attempts at excision and inoculation of the same patient with filtrates and macerated tumor tissue have been unsuccessful in transplanting this tumor. The disease evolves through three stages: an inflammatory macule, a granulomatous papule or nodule, and finally a true confluent neoplasm, of varied and complex structures, composed of the tissue elements (nerve, connective tissue, smooth muscle, endothelium) found in the intricate neurovascular annexes; hardly the simple form of tumor one would expect to develop from infection or inflammation.

*Precancerous Lesions.*—In the entire field of cancer prophylaxis no greater opportunity exists than in the case of epitheliomas of the hands and feet. It is not an exaggeration to say that practically all of them could be prevented. The abuse or excessive use of arsenical medication, excessive exposure to sunlight for many years, occupational dermatitis of the hands in workers with tar and oil products, the chronic irradiation of the hands of physicians and technicians employing x-rays and radium, improper early treatment of burns by failure to skin graft, and other causes contributory to scarring of the skin are uniformly preventable. It may require twenty or thirty years of such chronic irritation to induce these precancerous lesions of the skin, so that prophylaxis should be applied in early life and not delayed until later when the effects begin to be manifested. Once the pre-

cancerous changes in the skin are apparent, i.e., atrophy, hyperkeratosis, loss of oil and sweat glands, much can be done by careful hygiene of the hands. Keratoses may be treated by electrodesiccation or by beta irradiation (Fig. 12). Bland vegetable oils or animal fats should be applied to the dry skin. One precancerous state which cannot be prevented and which seems chiefly to involve the hands and feet is the so-called *acrodermatitis chronica atrophicans*. This disease is somewhat similar to *scleroderma*; the skin of the hands and feet, later of the forearms and legs, undergoes spontaneous progressive atrophy. The

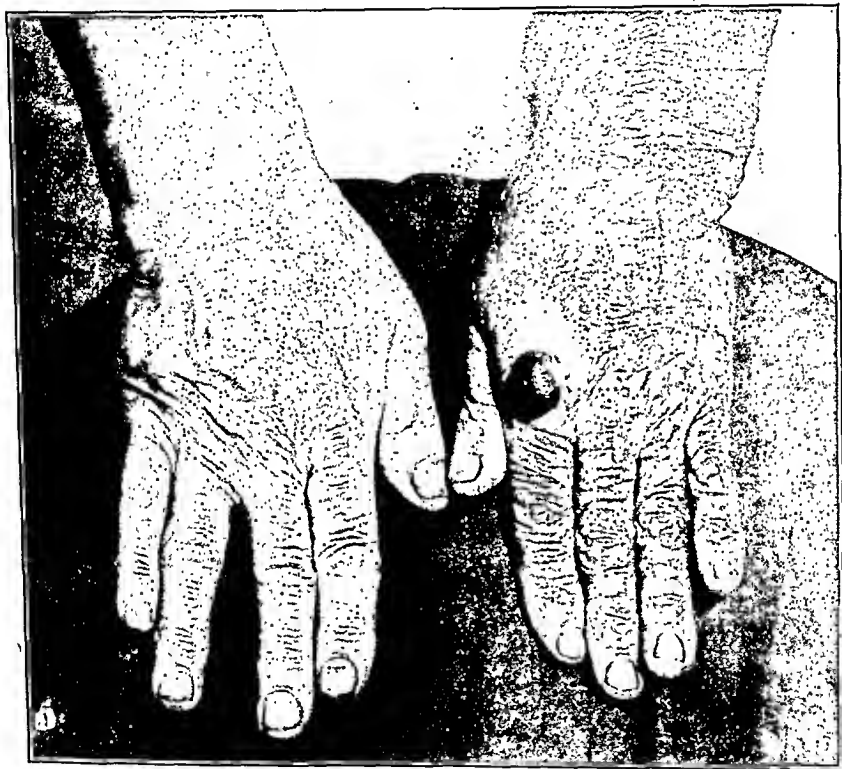


Fig. 1.—Spindle-cell epidermoid carcinoma developing in *acrodermatitis chronica atrophicans*. This precancerous disease is more marked on the left hand. Note the atrophy, transparency, and anetodermia.

skin becomes thin, violaceous, and transparent. The oil and sweat glands disappear, together with the elastic tissue. (Fig. 1.) In time epitheliomas, often multiple, develop and may metastasize early; they are occasionally of the spindle-cell type and have been known to metastasize by the blood stream to internal organs. All pigmented naevi of the hands and feet are subject to frequent trauma and therefore should be surgically excised while benign.

*Congenital Origin.*—There are at least five varieties of tumors of the hands and feet which are of congenital origin and can be satisfactorily explained by Cohnheim's theory of cell rests. One is the central

chondroma or enchondroma of the phalanges and metacarpal bones. Another is a rare cartilaginous tumor of the tendon sheath, occurring in multiple foci and often resembling abortive attempts to produce sesamoid bones (Fig. 2). A third is von Recklinghausen's type of generalized neurofibromatosis (Figs. 3 and 4). The hemangioma is a well-known congenital tumor (Figs. 5 and 6), as is the lipoma (Fig. 7).

*Role of Trauma.*—As previously stated, chronic irritation or repeated minor trauma has been accepted as a provocative cause of precancerous lesions and epitheliomas of the hands and feet. The evidence,

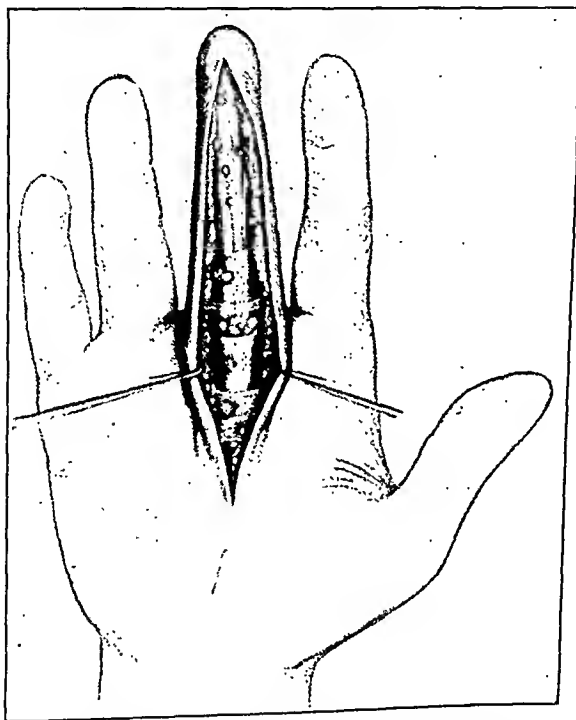
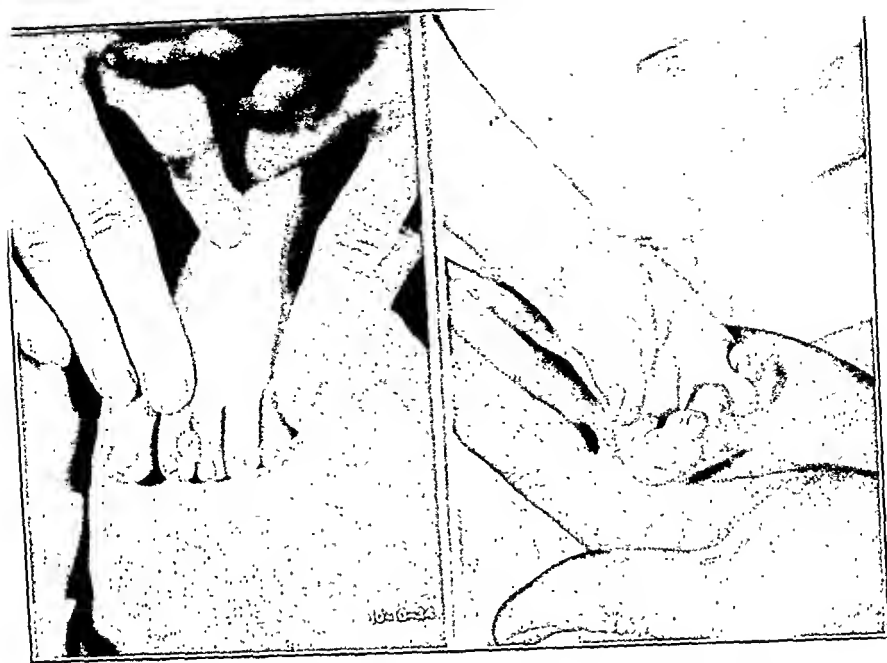


Fig. 2.—Multiple congenital benign chondromas of tendon sheath. They may have a histogenetic relationship to sesamoid bones.

especially in industrial workers, has been sufficiently conclusive to secure monetary compensation in court for such damages. A curious paradox exists in the case of the common corn or clavus, caused by chronic frictional irritation, a lesion that is markedly hyperkeratotic, yet having little or no tendency to become cancerous. A single or repeated injury to certain types of pigmented naevi may be responsible for their conversion into malignant melanomas, as testified by numerous clinical examples. Of greatest medicolegal importance, however, is the question whether or not a single trauma can induce a malignant tumor of the hands or feet. In seeking a solution to this problem, the



A.

B.

Fig. 3.—A, Neurofibroma of toe; B, multiple congenital neurofibromas of hand in same patient as shown in A; note contractural deformities so commonly occurring in this disease.



A.

B.

C.

Fig. 4.—A, Neurogenic sarcoma of low grade malignancy developing in hand, recurrent after excision. This patient had congenital neurofibromatosis of left hand and forearm. Note flexion and crossed deformities of fingers which was present at birth, a common neurogenic deformity. B, Dissected hand and wrist after amputation to show diffuse neurosarcoma of palm and wrist. C, Seven operations, including three amputations were done. Each time the diffuse neurosarcoma recurred higher up along the nerve trunks. An interscapulothoracic amputation was finally necessary. There has been no evidence of recurrence during the  $3\frac{1}{2}$  years intervening since this last operation.

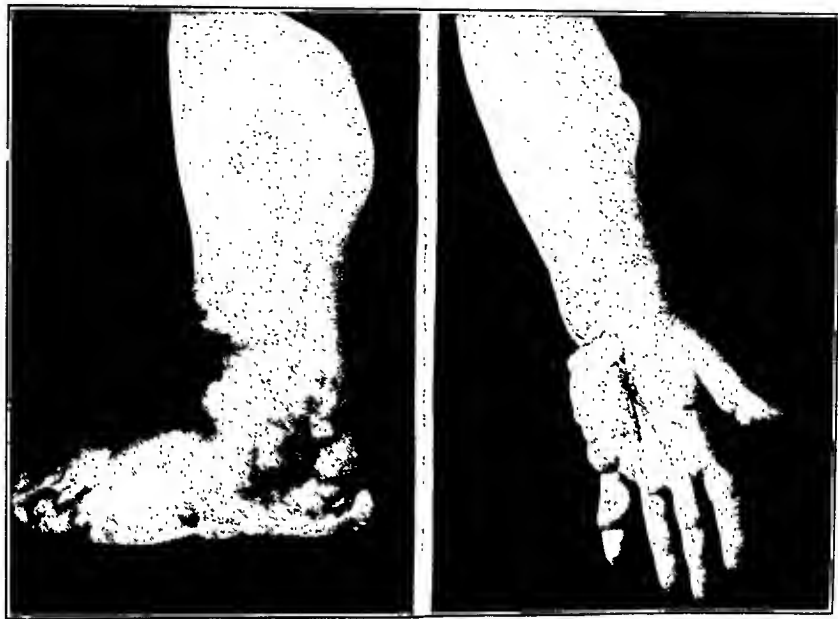


Fig. 5.—Congenital diffuse hemangiomatosis of hand and foot in same patient. There is a coexistent hypertrophy of bones of the foot. Radiographic examination of the foot indicates that the hemangioma involves bone.

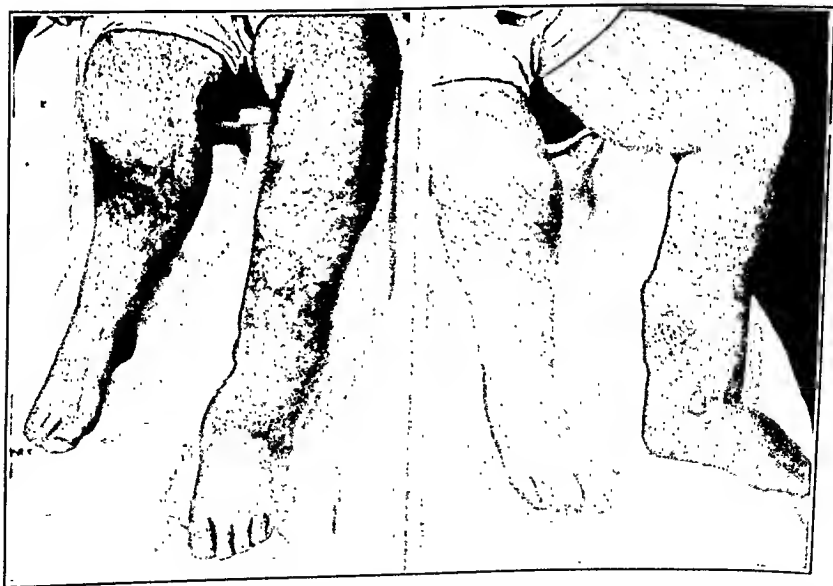
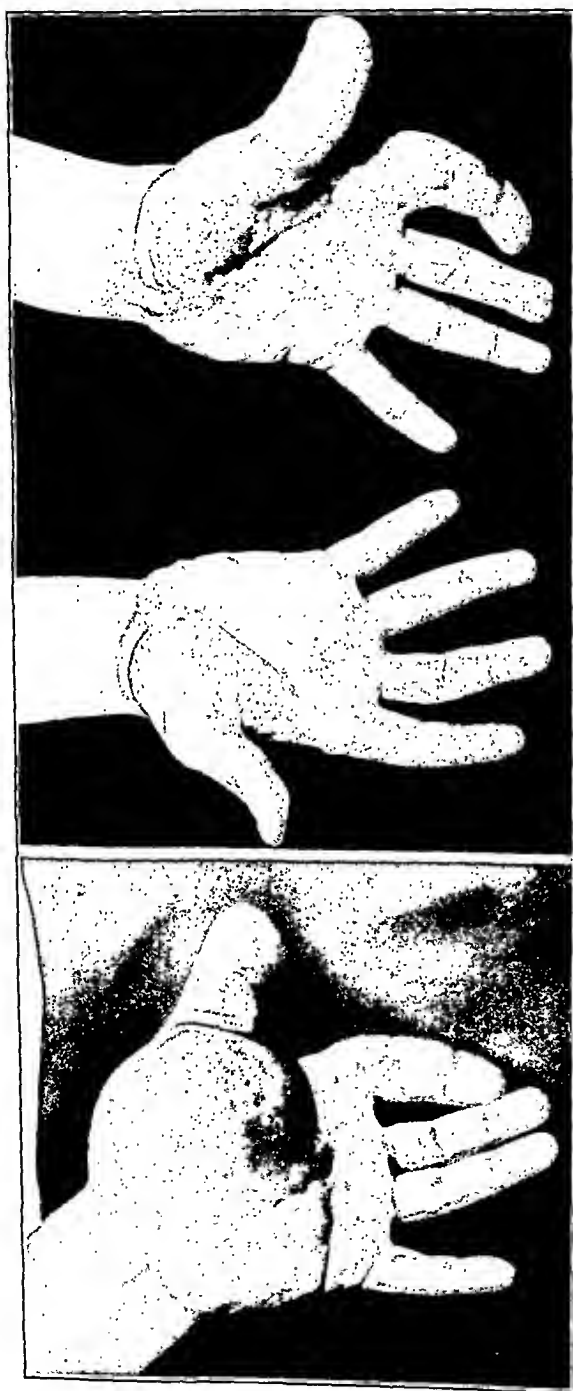


Fig. 6.—Congenital lymphangiomatosis of left foot and leg. Note the lymphangiectatic hyperkeratoses on medial aspect of left heel and between toes of left foot. The right leg is congenitally deformed, thus exaggerating the elephantiasis and overgrowth of long bones of the left lower leg. This phenomenon occurs occasionally with diffuse angiomatosis of an extremity. An ulcerating malignant endothelioma recently has developed on the medial aspect of the left ankle.



A.

B.

Fig. 7.—A, Congenital lipomatosis of left hand and arm. Note relative sizes of right and left thumbs and deformity of left forefinger. B, After surgical excision of lipoma in left thenar region.



examiner should apply the postulates of Ewing concerning (1) the authenticity and adequacy of the trauma, (2) the previous integrity of the wounded part, (3) the origin of the tumor at the exact point of injury, (4) a reasonable time limit between the injury and the appearance of the tumor, and (5) the type of tumor resulting. The only malignant bone tumor of the hands and feet which is generally accepted to have a traumatic basis is the subperiosteal sarcoma; the mechanism here is probably disruption of the periosteum from the cortex with an intervening hematoma, organization of the blood clot, and later neoplastic hyperplasia. The same *modus operandi* probably occurs in the two other malignant tumors of possible traumatic origin; namely, malignant synovioma and liposarcoma. Almost every patient having a synovioma will relate a history of injury which seems to be authentic and adequate. Here again hemorrhage accompanies laceration of tendon sheaths and joint capsules and the normal reparative processes in some instances go on to the formation of a true synovial tumor, usually malignant. Some liposarcomas are unquestionably caused by a single acute injury. The adult type of liposarcoma with opaque granular cells is the one that follows trauma. Just as hemorrhage in muscle may lead to organization, calcification, osteogenesis, and occasionally the formation of an osteosarcoma, the same process in fat may result either in traumatic fat necrosis and healing with or without calcification or the stimulation of the adult fat cells to grow diffusely as a sarcoma possessing many grades of anaplasia and malignancy. As Ewing has said: "This type of liposarcoma represents the lawless phase of the growth of fat cells observed to a lesser degree in chronic inflammation of fat tissue." Dupuytren's contracture is really a diffuse neuromatous tumor occurring in the palm of the hand and developing after repeated chronic injuries, usually of the bruising type.

#### INCIDENCE OF TUMORS OF THE HANDS AND FEET

For the twenty-one-year period, Jan. 1, 1917, to Jan. 1, 1938, there were 573 tumors of the hands and feet treated at the Memorial Hospital for Cancer and Allied Diseases. The distribution of these 573 malignant and benign tumors according to site is shown in Table I. The upper extremities are more commonly involved, with 247, or 43.1

TABLE I  
DISTRIBUTION OF MALIGNANT AND BENIGN TUMORS, ACCORDING TO SITE

SITE	TOTAL		MALIGNANT		BENIGN	
	NO.	%	NO.	%	NO.	%
Total	573	100.0	369	100.0	204	100.0
Hand	247	43.1	171	46.3	76	37.3
Finger	142	24.8	61	16.5	81	39.7
Foot	147	25.7	112	30.3	35	17.1
Toe	37	6.4	25	6.8	12	5.9

per cent, on the hand, and 142, or 24.8 per cent, on the fingers, together constituting more than two-thirds of all the tumors in this series. The largest proportion of the malignant tumors, 46.3 per cent, involves the hand, which might be expected from the fact that this site comprises the largest proportion of the total tumors.

Table II indicates the proportion of tumors at each site that are malignant and benign, with the foot showing the highest proportion among the malignant tumors of 76.2 per cent. In each regional location, with the exception of the fingers, the greater proportion of the tumors is malignant; phalangeal tumors, however, have a greater tendency to be benign, 57.0 per cent.

TABLE II

PROPORTION OF TUMORS AT EACH SITE WHICH ARE MALIGNANT AND BENIGN

SITE	TOTAL		MALIGNANT		BENIGN	
	NO.	%	NO.	%	NO.	%
Total	573	100.0	369	64.4	204	35.6
Hand	247	100.0	171	69.2	76	30.8
Finger	142	100.0	61	43.0	81	57.0
Foot	147	100.0	112	76.2	35	23.8
Toe	37	100.0	25	67.6	12	32.4

The various types of benign tumors of the hands and feet are shown in Table III. The largest proportion are papillomas (24.5 per cent) and angiomas (23.5 per cent). The giant cell tumor of tendon sheath (xanthoma) and pyogenic granuloma comprise 15.7 and 14.7 per cent, respectively, of the benign tumors.

TABLE III

DISTRIBUTION OF BENIGN TUMORS ACCORDING TO SITE AND TYPE OF TUMOR

TYPE OF TUMOR	TOTAL	HAND	FINGER	FOOT	TOE
Total	204	76	81	35	12
Chondroma	13	2	9	--	2
Giant cell tumor of tendon sheath (xanthoma)	32	12	17	3	--
Angioma, hemangioma, lymphangioma	48	19	16	12	1
Papilloma, cutaneous horn	50	24	17	8	1
Glomus tumor	5		5		
Lipoma	4	4			
Neuroma	22	10	2	8	2
Granuloma	30	5	15	4	6

The malignant tumors of the hands and feet are grouped in ten divisions, with the figures for the incidence of each type and site listed in Table IV. Epidermoid carcinoma comprised 180, or 48.8 per cent, of the 369 malignant tumors; two-thirds (124) of these cancers, or 68.9 per cent, were situated on the hands. The next largest group is the malignant melanoma, of which there were 105 tumors, or 28.5 per cent. In contrast to the epidermoid carcinoma, the largest proportion of melanomas were on the feet, 58 or 55.2 per cent.

TABLE IV

DISTRIBUTION OF MALIGNANT TUMORS ACCORDING TO SITE AND TYPE OF TUMOR

TYPE OF TUMOR	TOTAL	HAND	FINGER	FOOT	TOE
Total	369	171	61	112	25
Epidermoid carcinoma	180	124	32	20	4
Basal cell epithelioma	13	10	2	1	
Sweat gland carcinoma					
Adenoid cystic epithelioma					
Metastatic carcinoma	2	1	1		
Melanoma (malignant)	105	12	17	58	18
Osteogenic sarcoma	8	2	1	3	2
Periosteal sarcoma					
Chondrosarcoma					
Endothelial myeloma	1			1	
Malignant synovioma	19	7	4	8	
Endothelioma of tendon sheath					
Neurogenic sarcoma	15	7	1	7	
Sarcoma of undetermined histogenesis: fibrosarcoma myxosarcoma	16	7	3	6	
Kaposi's sarcoma	10	1		8	1

## CURABILITY OF TUMORS OF THE HANDS AND FEET

Many difficulties attend any attempt to analyze the end results of treatment of malignant tumors of the hand and feet. Each histologic type should be considered as an entity. The results vary also with the degree of anaplasia, the local extent or depth of infiltration, the presence of metastases in regional lymph nodes, the tendency to visceral involvement, the coexistence or later development of multiple tumors

TABLE V

PROPORTION OF MALIGNANT TUMORS OCCURRING ON THE HAND AND FOOT

TYPE OF TUMOR	TOTAL CASES	HAND AND FOOT	
	ENTIRE BODY	NO.	%
Epidermoid carcinoma of skin (exclusive of genitals and lip)	1,584	180	11.6
Basal cell epithelioma	2,189	13	0.6
Malignant melanoma	481	105	21.8
Osteogenic sarcoma	644	8	1.2
Malignant synovioma	99	19	19.3
Endothelioma of tendon sheath			
Neurogenic sarcoma	484	15	3.9
Sarcoma unclassified	204	16	7.8

of the same type in the same patient, the inherent incurability of a disease that is of generalized distribution, and the age of the patient. An epithelioma that has invaded the deep fascia and become fixed will require more radical treatment than one which is confined to skin and is readily movable. The metastatic involvement of regional lymph nodes by malignant melanoma and epidermoid carcinoma unfavorably influences the prognosis; radical axillary or groin dissection is necessary to supplement the treatment of the primary lesion. Pulmonary metastasis may occur so early in the history of osteosarcoma and ma-

lignant synovioma as to nullify the good effect of local treatment, however radical. In the case of Kaposi's idiopathic sarcoma, any single nodule can be destroyed, but the slow progressive generalization of the disease is so inevitable that control rather than cure is the object of treatment.

The regional location of these malignant tumors is peculiarly favorable for curative treatment either by surgical or radiologic means, as indicated. Conservative surgical measures sparing a functional part of the foot or hand sometimes are possible.

The end results of treatment of epidermoid carcinomas of the hands and feet are really better than the figures herein submitted. Epitheliomas of the extremities occur at an average age almost ten years older than in epitheliomas of the face and lip. These elderly patients, many of whom are more than 70 years old, are difficult to keep under observation; they may die of intercurrent diseases while under treatment or before the five-year period which is generally accepted as the criterion for cure has passed. For example, in Table VI, dealing with the end results of epidermoid carcinomas of the hands and feet, 82 patients were lost to observation and analysis. Of this group, 53 patients either received no treatment, refused treatment, were treated elsewhere, or did not complete the treatment outlined at the Memorial Hospital. Of the remaining 39 patients who were treated but subsequently could not be found, 19 were clinically free of cancer more than two years after treatment and 11 were known to have no evidence three or more years after treatment had been instituted.

TABLE VI  
EPIDERMOID CARCINOMAS OF HANDS AND FEET  
END RESULTS OF TREATMENT

END RESULTS	NUMBER	PER CENT
Total patients	180	
Lost to observation	82	
Number available for study of end results	98	100.0
Dead	36	36.7
Living with evidence (total)	13	13.2
Less than 5 yr.	9	9.2
5 or more yr.	4	4.1
Living with no evidence (total)	49	50.0
Less than 5 yr.	19	19.3
5 to 10 yr.	26	26.4
10 or more yr.	4	4.1

*End Results of Epitheliomas of Hands and Feet Metastatic to Regional Lymph Nodes.*—Theoretically all epitheliomas of the hands and feet should be cured before metastasis occurs, if our statistics are correct, as they reveal the fact that the average interval between the first appearance of the carcinoma and the recognition of nodal metastasis is three years. The decision to be made concerning prophylactic

TABLE IV

DISTRIBUTION OF MALIGNANT TUMORS ACCORDING TO SITE AND TYPE OF TUMOR

TYPE OF TUMOR	TOTAL	HAND	FINGER	FOOT	TOE
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Periosteal sarcoma					
Chondrosarcoma					
Endothelial myeloma	1			1	
Malignant synovioma	19	7	4	8	
Endothelioma of tendon sheath					
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series of 17 axillary dissections for metastatic carcinoma of the hand, 6 (35 per cent) of these patients subsequently died and 11 are now living and well; 5 of this group were operated upon more than five years ago. Of 7 inguinal dissections for metastatic carcinoma of the foot, 2 of these patients are dead and 5 are living and well; 3 of this group were operated upon more than five years ago.

TABLE X  
MALIGNANT MELANOMA OF HANDS AND FEET  
END RESULTS IN RELATION TO SITE OF TUMOR

END RESULTS	HAND		FINGER		FOOT		TOE	
	NO.	%	NO.	%	NO.	%	NO.	%
Total patients	12		17		58		18	
Lost to observation	3		3		10			
No. available for study of end results	9	100.0	14	100.0	48	100.0	18	100.0
Dead (total)	3	33.3	5	35.7	37	77.0	13	72.2
Living with evidence	3	33.3	3	21.4	3	6.3	2	11.1
Living with no evidence	3	33.3	6	42.9	8	16.7*	3	16.7

\*In contradistinction to the epidermoid carcinomas, the incidence of melanomas is greater on the foot than on the hand. The curability of melanomas of the foot is only one-half as great as the curability of melanomas of the hand. It has long been known that the prognosis of melanoma of the foot is worse than for melanoma of the hand.

*End Results of Melanomas of Hands and Feet Metastatic to Regional Lymph Nodes.*—In a series of 32 axillary dissections for metastatic melanoma of the upper extremities (including arm and forearm as well as hand), 19 of these patients subsequently died and 13 are living and well; 4 of this group were operated upon more than five years ago. In a similar series of 31 inguinal dissections for metastatic melanoma of the lower extremities, 24 of these patients are now dead and only 7 are living and well; 5 of this group have fulfilled the criterion of five-year cure. Twenty-six patients received radiation therapy as the sole method of treatment of metastatic melanoma in inguinal and axillary lymph nodes. Such treatments consisted of combinations of external irradiation with high voltage x-rays or radium element pack and interstitial radium therapy. Only 2 of these 26 patients are now living and without clinical evidence of metastatic melanoma; the periods of observation, however, are less than three years.

The distinction between radiosensitive and radioresistant tumors of the hands and feet is not absolute. In this connection it should be noted that radiosensitivity and radiocurability are not synonymous terms. A radiosensitive tumor, such as lymphosarcoma, may respond phenomenally well to irradiation, yet destroy the patient because of early and widespread metastases. On the other hand, certain slow-growing and radioresistant fibrosarcomas may slowly but completely regress after long-continued irradiation.

TABLE VII  
EPIDERMOID CARCINOMAS OF HANDS AND FEET  
END RESULTS IN RELATION TO SITE OF TUMOR

END RESULTS	HAND		FINGER		FOOT		TOE	
	NO.	%	NO.	%	NO.	%	NO.	%
Total patients	124		32		20		4	
Lost to observation	60		15		7			
No. available for study of end results	64	100.0	17	100.0	13	100.0	4	100.0
Dead	24	37.5	7	41.2	3	23.0	2	50.0
Living with evidence	4	6.3	3	17.6	6	46.2		
Living with no evidence	36	56.2	7	41.2	4	30.8	2	50.0

dissection of regional lymph nodes when there is no clinical evidence of their involvement must be influenced by the fact that 24 per cent

TABLE VIII  
END RESULTS OF TREATMENT FOR MISCELLANEOUS TUMORS OF HANDS AND FEET

END RESULTS	TYPES OF TUMOR			
	SARCOMA	UNCLASSIFIED	SYNOVIOMA	NEUROSARCOMA
Total patients		16	19	15
Lost to observation		7	5	7
No. available for study of end results		9	14	8
Dead (total)		5	4	1
Living with evidence (total)		1	7	1
Within 1 yr. of admission	1		3	
1 to 5 yr.			3	1
5 or more yr.			1	
Living with no evidence (total)		3	3	6
Within 1 yr. of admission	1			1
1 to 5 yr.	1		2	5
5 or more yr.	1		1	

of our patients admitted with epidermoid carcinomas of the hands and feet and without palpable lymph nodes in axilla and groin subsequently developed nodal metastases while under observation. In a

TABLE IX  
MALIGNANT MELANOMA OF HANDS AND FEET  
END RESULTS OF TREATMENT

END RESULTS	NUMBER		PER CENT
Total patients	105		
Lost to observation	16		
No. available for study of end results	89		100.0
Dead (total)	58		65.1
Living with evidence (total)	11		12.4
Within 1 yr. of admission	5	5.6	
Over 1 yr.	6	6.7	
Living with no evidence (total)	20		22.4
1 to 3 yr.	4	4.5	
3 to 5 yr.	7	7.9	
5 to 10 yr.	7	7.9	
10 or more yr.	2	2.2	

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TABLE X  
MALIGNANT MELANOMA OF HANDS AND FEET  
END RESULTS IN RELATION TO SITE OF TUMOR

END RESULTS	HAND		FINGER		FOOT		TOE	
	NO.	%	NO.	%	NO.	%	NO.	%
Total patients	12		17		58		18	
Lost to observation	3		3		10			
No. available for study of end results	9	100.0	14	100.0	48	100.0	18	100.0
Dead (total)	3	33.3	5	35.7	37	77.0	13	72.2
Living with evidence	3	33.3	3	21.4	3	6.3	2	11.1
Living with no evidence	3	33.3	6	42.9	8	16.7*	3	16.7

\*In contradistinction to the epidermoid carcinomas, the incidence of melanomas is greater on the foot than on the hand. The curability of melanomas of the foot is only one-half as great as the curability of melanomas of the hand. It has long been known that the prognosis of melanoma of the foot is worse than for melanoma of the hand.

*End Results of Melanomas of Hands and Feet Metastatic to Regional Lymph Nodes.*—In a series of 32 axillary dissections for metastatic melanoma of the upper extremities (including arm and forearm as well as hand), 19 of these patients subsequently died and 13 are living and well; 4 of this group were operated upon more than five years ago. In a similar series of 31 inguinal dissections for metastatic melanoma of the lower extremities, 24 of these patients are now dead and only 7 are living and well; 5 of this group have fulfilled the criterion of five-year cure. Twenty-six patients received radiation therapy as the sole method of treatment of metastatic melanoma in inguinal and axillary lymph nodes. Such treatments consisted of combinations of external irradiation with high voltage x-rays or radium element pack and interstitial radium therapy. Only 2 of these 26 patients are now living and without clinical evidence of metastatic melanoma; the periods of observation, however, are less than three years.

The distinction between radiosensitive and radioresistant tumors of the hands and feet is not absolute. In this connection it should be noted that radiosensitivity and radiocurability are not synonymous terms. A radiosensitive tumor, such as lymphosarcoma, may respond phenomenally well to irradiation, yet destroy the patient because of early and widespread metastases. On the other hand, certain slow-growing and radioresistant fibrosarcomas may slowly but completely regress after long-continued irradiation.



RADIATION THERAPY OF TUMORS OF HANDS AND FEET  
CLASSIFICATION OF RADIOSENSITIVITY

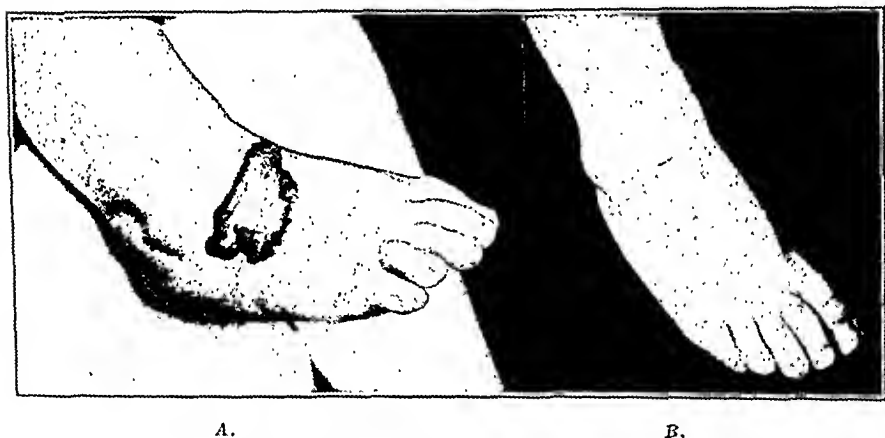
TABLE XI  
CLASSIFICATION OF RADIOSENSITIVITY

RADIOSENSITIVE	RADIORESISTANT
<i>Benign Tumors</i>	
Wart	Fibroepithelial tumor
Epithelial papilloma	Neuroma
Hemangioma	Lipoma
Granuloma	Neurofibroma
	Lymphangioma
	Glomus tumor
	Giant cell tumor of tendon sheath (xanthoma)
	Chondroma
	Osteoma
<i>Malignant Tumors</i>	
Epidermoid carcinoma	Osteosarcoma
Basal cell carcinoma	Melanoma
Kaposi's sarcoma	Spindle cell sarcoma
Endothelial myeloma	Myxosarcoma
	Neurosarcoma
	Synovioma

None of the nine common benign tumors in the radioresistant group should ever be treated by any form of radiation therapy. Epithelial warts and papillomas readily regress after small doses of unfiltered low voltage x-radiation, or by the application of the beta ray of radium applied through the medium of a radon bulb (Fig. 12). The hemangiomas vary greatly in radiosensitivity; the cavernous hemangiomas regress by thrombosis, organization, and obliteration (Fig. 8) following the surface application of radium or low voltage x-rays. In the more radioresistant hemangiomas, small doses of interstitial radium therapy, either by gold radon seeds or radium element needles, may be necessary to complete the disappearance of tumor. Hemangiomas, as a rule, are much more radiosensitive in infancy than they are in childhood and later life; with added years, the endothelial cells and blood vessels comprising the tumor lose their embryonal and therefore radiosensitive character. Pyogenic granulomas, occurring quite frequently in the nail sulci, are not readily amenable to surgical treatment because of the frequency of recurrence; small doses of lightly filtered radiation, either by low voltage x-rays or radium, will suffice to cause complete disappearance of this tumor with practically no discernible scar.

In the group of malignant tumors of the hands and feet, radiation therapy should never supplant surgical excision or amputation as the sole method of treatment of osteosarcoma, malignant melanoma, spindle cell sarcoma, and myxosarcomas of undetermined histogenesis. If the

sarcomas are inoperable, radiation therapy may afford some palliation by the exercise of growth restraint. Radical surgical treatment is the method of choice for most neurosarcomas and malignant synoviomas, but irradiation is often a useful adjunct to surgical treatment, being used either preoperatively or postoperatively, or both. Some cures have been effected by radiation therapy alone, but the prospect of cure is not great. After careful fractionated irradiation by high voltage roentgen rays, the neurosarcomas and malignant synoviomas may slowly diminish in size; this regression is never dramatic in its rapidity, but it is a progressive, gradual replacement of the tumor by dense, fibrous tissue producing a condition termed by Ewing "abortive fibrosis" (Fig. 9). Although the operative wounds made following such radiation therapy are of slow healing, the end result may justify such pre-operative irradiation, as local recurrence is seldom the rule.



A.

B.

Fig. 8.—A, Congenital hemangioma of dorsum of foot; B, result of radiation therapy.

The superficial epidermoid carcinomas and the less frequent basal cell epitheliomas of the hands and feet readily can be cured by the application of radium plaques (Fig. 11) or by contact or short distance low voltage roentgen therapy (Fig. 10) or by the usual method of low voltage roentgen therapy. Although radiation cures of these tumors are possible of accomplishment, this method is not always indicated, as there is great danger of late radiation necrosis, particularly if the cancers are situated on the dorsum of the hand or foot in close proximity to bone, where there is not an abundance of underlying soft tissues. It is for this reason that many of the epitheliomas of hands and feet are better treated by surgical excision and skin grafting. With improvement in the technique of radiation therapy, particularly the new modalities that have recently come into use, and with full appreciation of the hazards encountered, the radiologist may secure

good results, providing the epithelioma does not infiltrate into tendon or bone.

The endothelial myeloma, or Ewing's tumor of bone, as a rule is quite radiosensitive, diminishing early and rapidly after exposure to roentgen rays. The immediate and seemingly complete clinical disappearance of this tumor may give one a false impression of security, because it is usually found that even intensive irradiation does not completely sterilize the endothelial myeloma. On this account, it is deemed imperative in most instances to follow such irradiation by amputation in those cases where the tumor has a single focus in bone. Wherever there are multiple endothelial myelomas, then, of course,

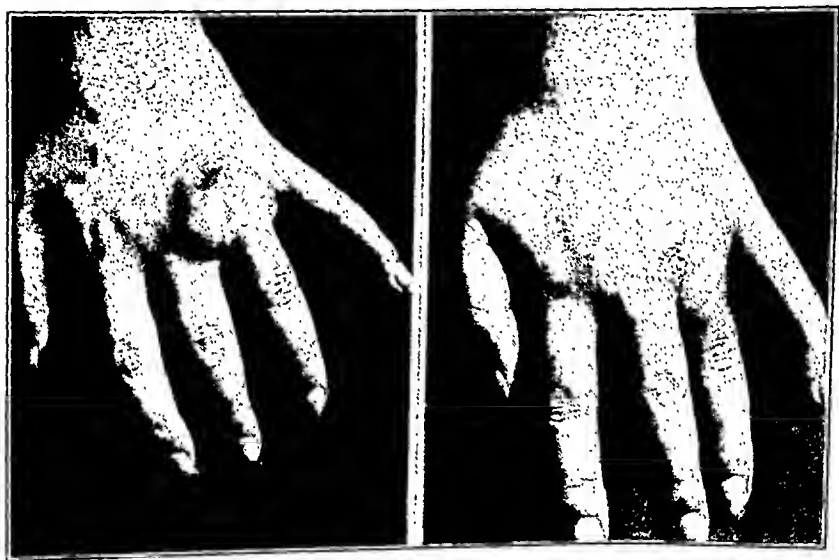


Fig. 9.—A, Recurrent adherent malignant synovioma, occurring in a young pregnant woman. B, Complete clinical regression following high voltage roentgen therapy. The factors were: 200 kv., 35 cm. target-skin distance, 0.5 mm. Cu + mm. Al filter, circular cone delimiting field as shown, anterior and posterior cross-firing fields, 300 r. units daily, alternating until each field received 3,600 r. units.

the possible curative value of amputation must be denied the patient in favor of the known palliative effect of roentgen therapy.

Inasmuch as the idiopathic hemorrhagic sarcoma of Kaposi is of multieentric origin, attempts at surgical control usually are futile. As many as five to ten, or even twenty, of these independent primary tumors may develop at the same time on both lower extremities. These nodules are not secondary extensions of a single primary sarcoma, but represent new independent foci of the disease which have a common underlying basis. It is well known that these sarcomas develop usually on the lower extremities of middle-aged men, the majority of whom have some circulatory disturbances. In one sense it is a generalized

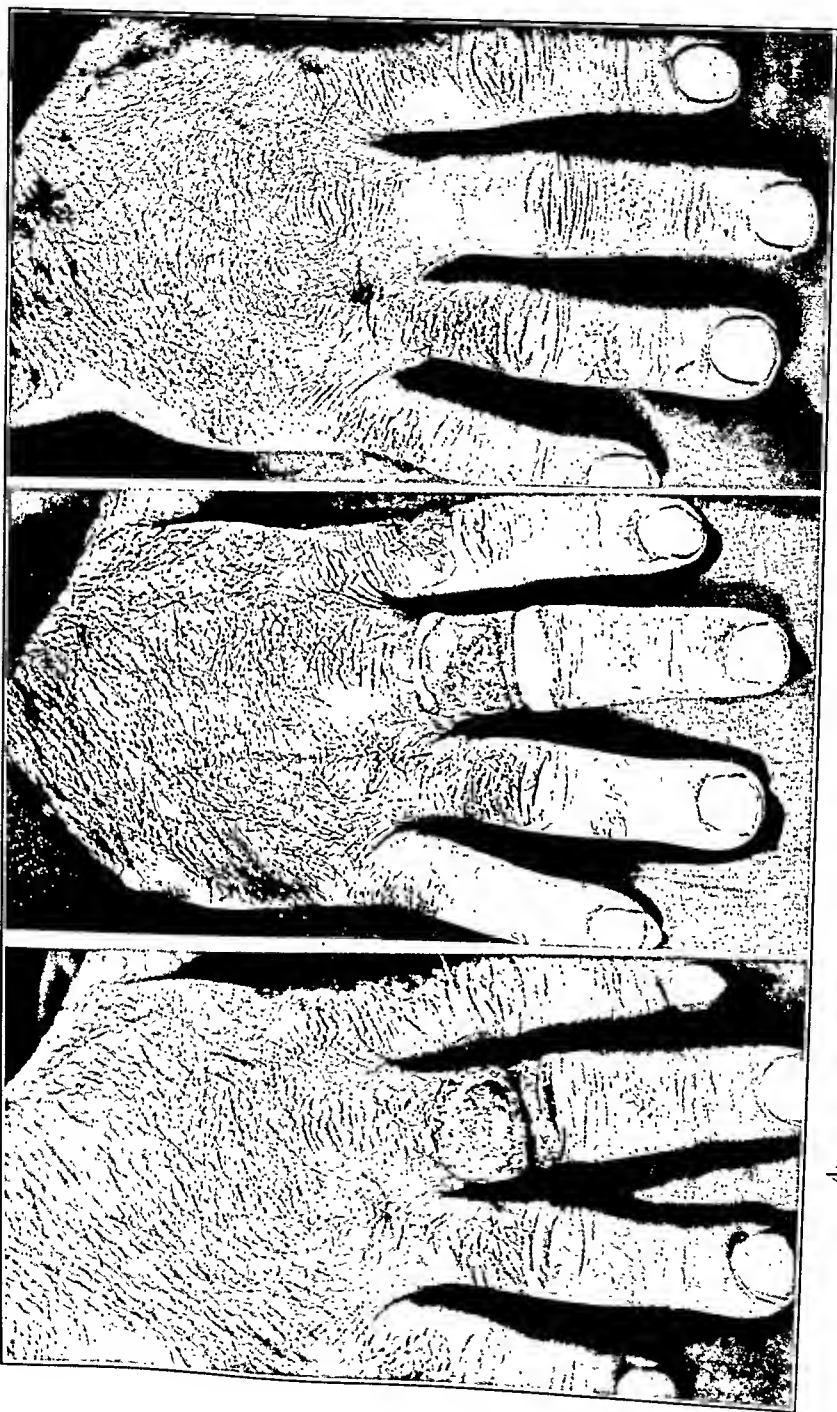


Fig. 10—4, Epidermoid carcinoma of skin of finger. An occupational cancer occurring in a mechanic whose hands were constantly immersed in tar and oil (July 31, 1936). *A*, Height of radiation reaction (Sept. 11, 1936). After low-voltage x-ray therapy, using the following factors: 100 kv., 30 cm. target-skin distance, 3 mm. Al filter, size of field as shown in illustration, 250 r. units daily to single port for total dose of 4,000 r. units. *C*, Result after healing (Dec. 4, 1936).

or systemic disease, although it may require years for the remainder of the body to be involved. This being the case, radiation therapy is definitely indicated as the sole method of treatment. Kaposi's sarcomas vary greatly in their histologic make-up, due to the fact that they originate from such a complex structure; namely, the neurovas-

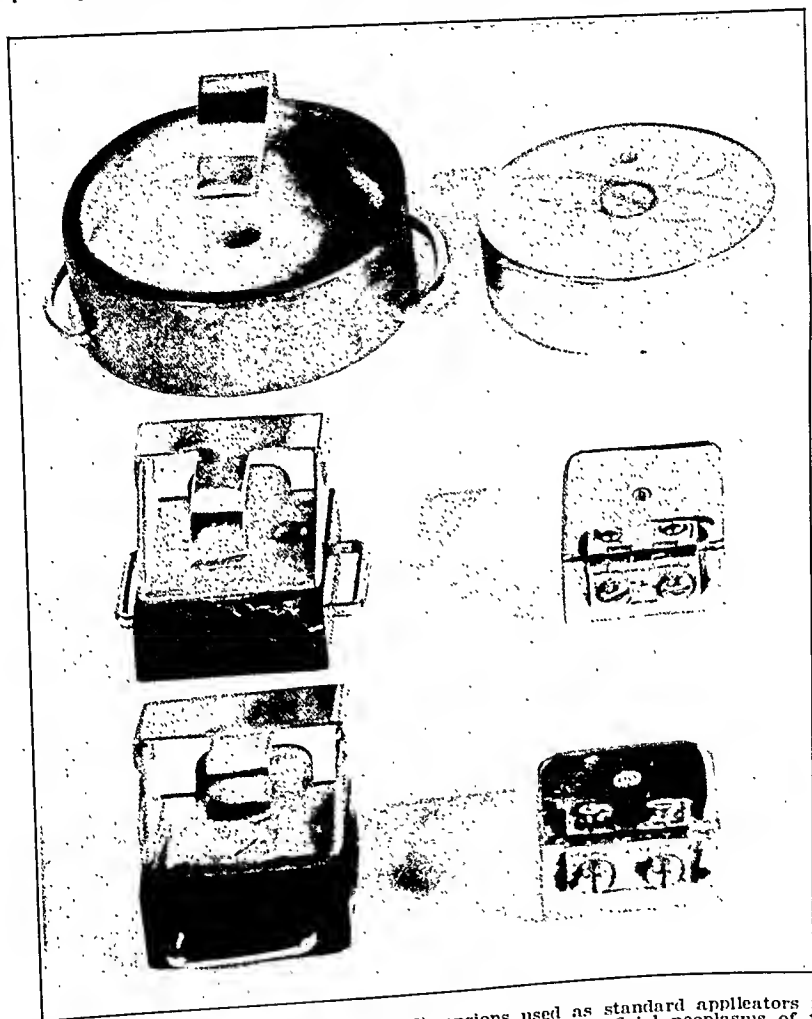


Fig. 11.—Radium plaques of various dimensions used as standard applicators for hemangiomas, epitheliomas, Kaposi's tumors, and other superficial neoplasms of the hands and feet. The bakelite blocks with safety catches are first applied over the tumor and furnish a radium skin distance of 1 cm., after which the radium plaques are slipped onto the blocks with a minimum of handling.

cular annexes in the skin and subcutaneous tissues. Hence, some of them are more angiomatous, others are neurosarcomatous, etc. Low voltage roentgen therapy, the topical application of radium by means of plaques applied at short distances, and contact radiation with low voltage x-rays or a radon bulb afford satisfactory methods of control.

## EQUIPMENT FOR RADIATION THERAPY OF TUMORS OF THE HANDS AND FEET

*Radium Therapy.*—The superficial tumors of the skin, e.g., epitheliomas, Kaposi's sarcoma, hemangioma, may be treated by standardized radium applicators of variable sizes. There are four standard radium applicators in general use at the Memorial Hospital and their different surface areas render them suitable for treating many small tumors of the skin and subcutaneous tissues (Fig. 11). The filtration of these plaques is the equivalent of 3 mm. brass. They are applied at a radium skin distance of 1 cm. with the exception of the tray which has a radium skin distance of 3 cm. Small blocks of balsa wood or bakelite are used to maintain this distance. The region surrounding the cancer is shielded by heavy lead to protect the normal adjacent tissues.

TABLE XII

TYPE	SIZE	AREA RADIATING SURFACE	FILTER	DIS- TANCE	DOSE MG. HR.
Square plaque	1.8 cm. square	2 sq. cm.	2 mm. brass + 0.2 mm. Pt.	1 cm.	700-1,000
Long plaque	2.7 × 1.7 cm.	3.75 sq. cm.	2 mm. brass + 0.2 mm. Pt.	1 cm.	900-1,200
Round plaque	4 cm. diameter	7 sq. cm.	2 mm. brass + 0.2 mm. Pt.	1 cm.	1,200-1,600
Tray	6.2 cm. diameter	17.5 sq. cm.	2 mm. brass + 0.2 mm. Pt.	3 cm.	3,000-4,000

*Gold Radon Seeds.*—These radon seeds for interstitial irradiation are 4 mm. long. They contain variable quantities of radon, usually 1.2 to 3 mc. per seed. The seeds are inserted into tumors using sterile precautions and they remain permanently in the tumor long after the radon has been completely dissipated. The dose necessary for tumors of various diameters, depending on the number of threshold erythema units required, is given in Table XIII. The figures in the table are true only when the radon is implanted in the central half of the tumor mass; if radon seeds are placed throughout the tumor at intervals of 1 cm., the quantity of radon employed should be increased by 25 per cent in order to arrive at the same dose in threshold erythema units. Gold radon seeds are indicated whenever interstitial radon is desired as an adjunct to contact or short distance radium or roentgen therapy. Care must be taken that the seeds are not inserted too near cartilage or bone, else a painful and chronic perichondritis or periostitis may follow.

or systemic disease, although it may require years for the remainder of the body to be involved. This being the case, radiation therapy is definitely indicated as the sole method of treatment. Kaposi's sarcomas vary greatly in their histologic make-up, due to the fact that they originate from such a complex structure; namely, the neurovas-

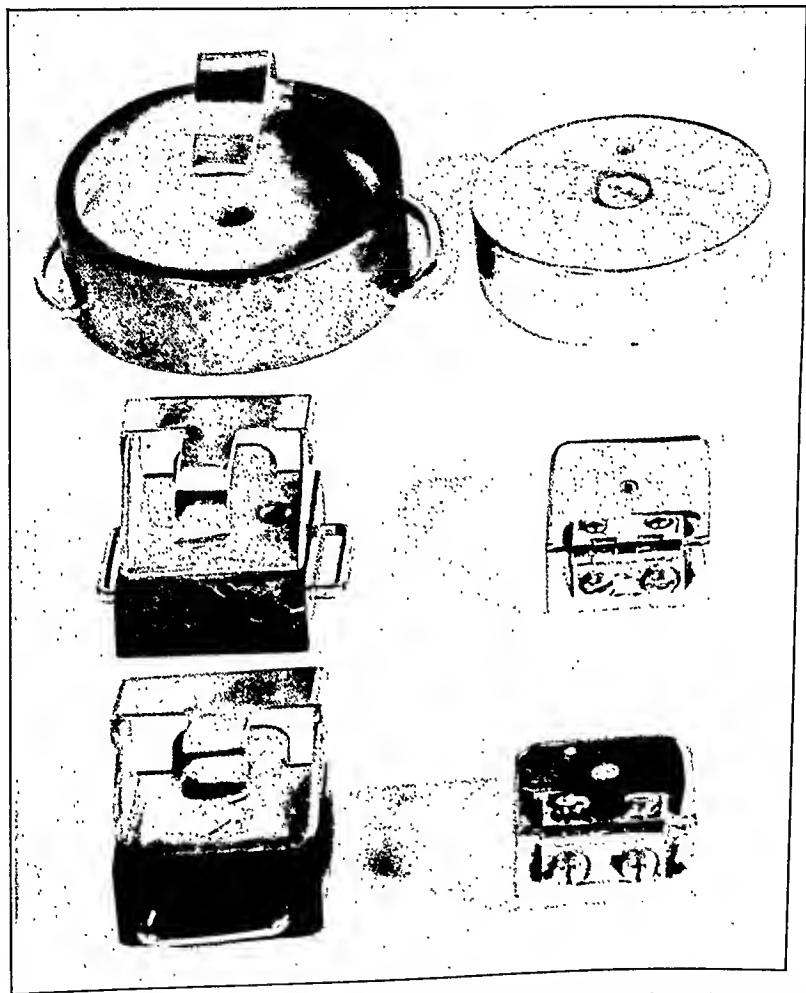


Fig. 11.—Radium plaques of various dimensions used as standard applicators for hemangiomas, epitheliomas, Kaposi's tumors, and other superficial neoplasms of the hands and feet. The bakelite blocks with safety catches are first applied over the tumor and furnish a radium skin distance of 1 cm., after which the radium plaques are slipped onto the blocks with a minimum of handling.

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plaster or by contact pressure from the various sized cylinders which are attached to the open port for the purpose of limiting the field of irradiation. Correction in the roentgen dose at the surface must be made when these shields and cones are used, because only the central portion of the beam is utilized. It is a well known physical law that the smaller the field, the less the depth dose obtained, due largely to a decrease in the scattered tissue radiation. Daily fractionated doses of 150, 200, or 250 roentgens are given until the total dose approximates 2,500 to 4,000 roentgens for malignant tumors. For hemau-

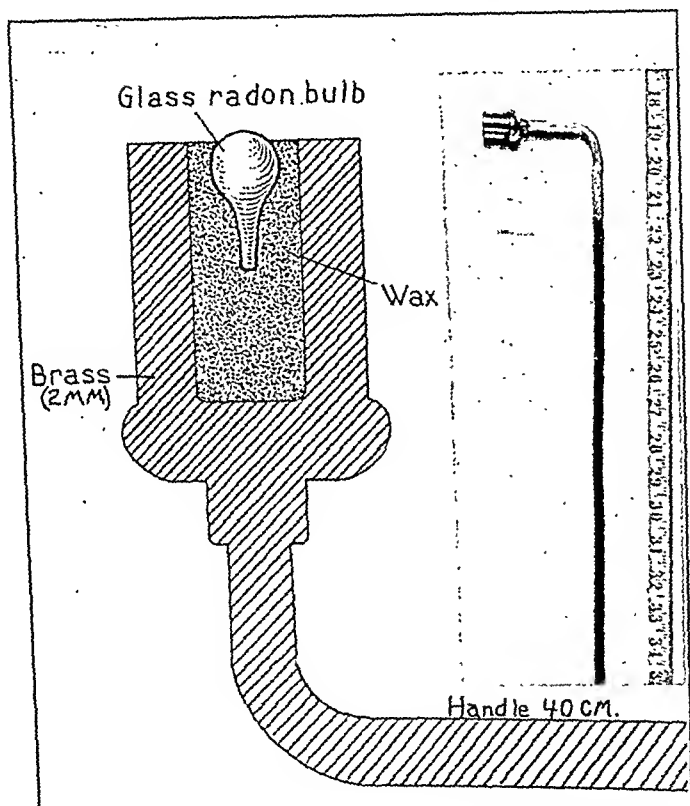


FIG. 12.—Radon bulb. This is made up once in three weeks at the Memorial Hospital. Since glass is used as a filter, the emanation is about 97 per cent beta and 3 per cent gamma. Its use is therefore restricted to very small and superficial basal cell carcinomas less than 1 mm. in thickness and precancerous lesions. Dosage is in "millicurie minutes," and varies between 200 and 600.

giomas doses of 150 to 300 roentgens may be given at weekly intervals for total doses seldom amounting to more than 1,500 r. units.

*Chaoul Contact or Short Distance Roentgen Therapy.*—During the past decade, physicists and radiologists have devoted considerable attention to the construction of low voltage x-ray machines which combine the advantages of radium dose distribution (as used for surface application) and the economy, efficacy, and convenience of the x-rays. Special x-ray tubes furnishing a dose distribution similar to contact



TABLE XIII

QUANTITIES OF RADIATION NECESSARY TO DELIVER SPECIFIED MINIMUM DOSES IN VARIOUS VOLUMES\* INTERSTITIAL SOURCES, FILTER 0.3-0.5 MM. GOLD

THRESHOLD DOSES	VOLUME (c.c.)						
	10	20	30	40	60	80	100
	<i>Mc. or Mg. Hr.</i>						
1	275	380	470	530	650	750	845
2	550	760	940	1060	1300	1500	1690
3	825	1140	1410	1590	1950	2250	2535
4	1100	1520	1880	2120	2600	3000	3380
5	1375	1900	2350	2650	3250	3750	4225
7	1925	2660	3290	3710	4550	5250	5915
10	2750	3800	4700	5300	6500	7500	8450

\*These doses are for needles to be left in place four days or longer. If they are to be removed in a shorter time, all quantities of radiation should be somewhat smaller (Quimby; Am. J. Roentgenol.).

*Radon Bulb.*—Radon in the quantity of 300 to 600 mc. is collected at intervals and pumped into a small glass sphere, which is imbedded in a wax cup at the end of a long handle (Fig. 12). This glass radon sphere or bulb is placed in direct contact with lesions of the skin to give doses, varying from 150 to 500 mc. minutes. As glass is the only filter, the radiation emitted is about 97 per cent beta rays and 3 per cent gamma rays. The use of this applicator therefore is limited to precancerous lesions of the skin, particularly keratoses.

*High voltage roentgen rays* with peak kilovoltage of 200 or more are seldom used in the treatment of skin cancers, except for deeply infiltrating epitheliomas. The more deeply situated synoviomas, neurosarcomas, fibrosarcomas, and bone tumors are treated by this modality for the indications previously mentioned. Limitation or restriction of the field of irradiation, cross-firing through dorsal and palmar or solar surfaces, and administration of daily small fractionated doses are the principles of treatment now almost universally adopted.

*Low voltage roentgen rays* of 100 to 140 peak kilovolts are important in the treatment of superficial benign and malignant tumors of the extremities, particularly epitheliomas. A target skin distance of 20 to 30 cm. is used, either without a filter or with 1 to 3 mm. of aluminium added, depending on the depth dose desired. Higher voltages, greater target skin distance, and heavier filters are indicated whenever an increased depth dose is needed for thick or deeply infiltrating cancers. Lower voltage, shorter target skin distance, and less filter or no filter at all are indicated for the superficial tumors. The normal skin surrounding the tumor to be treated is shielded with lead during an x-ray treatment. If x-rays of low intensity (100 kv.) are used, 1 mm. of lead will remove 99 plus per cent of the radiation, thus allowing ample protection. This thin sheet lead is easily cut and moulded to fit each individual epithelioma or hemangioma. The lead protective shields, when made, are then held in place with adhesive

plaster or by contact pressure from the various sized cylinders which are attached to the open port for the purpose of limiting the field of irradiation. Correction in the roentgen dose at the surface must be made when these shields and cones are used, because only the central portion of the beam is utilized. It is a well known physical law that the smaller the field, the less the depth dose obtained, due largely to a decrease in the scattered tissue radiation. Daily fractionated doses of 150, 200, or 250 roentgens are given until the total dose approximates 2,500 to 4,000 roentgens for malignant tumors. For heman-

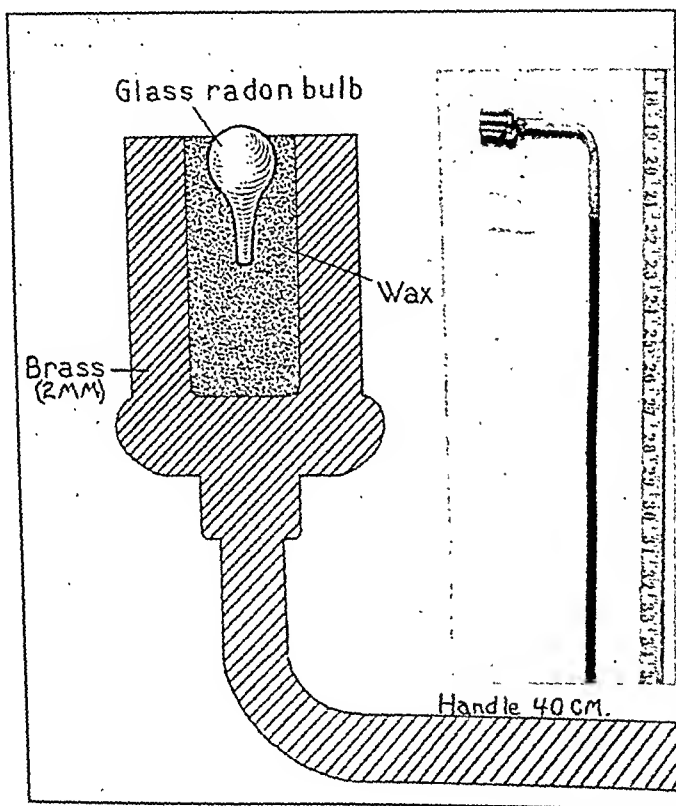


Fig. 12.—Radon bulb. This is made up once in three weeks at the Memorial Hospital. Since glass is used as a filter, the emanation is about 97 per cent beta and 3 per cent gamma. Its use is therefore restricted to very small and superficial basal cell carcinomas less than 1 mm. in thickness and precancerous lesions. Dosage is in "millicurie minutes," and varies between 200 and 600.

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*Chaoul Contact or Short Distance Roentgen Therapy.*—During the past decade, physicists and radiologists have devoted considerable attention to the construction of low voltage x-ray machines which combine the advantages of radium dose distribution (as used for surface application) and the economy, efficacy, and convenience of the x-rays. Special x-ray tubes furnishing a dose distribution similar to contact

or superficial radium therapy were designed many years ago and then abandoned because of technical difficulties concerned with the prevention of shock to the patient. These difficulties were subsequently overcome and the short-distance or contact x-ray method was developed. Schaefer and Witte, of Göttingen, Germany, experimented in 1929 using a Lenard tube and cathode rays only; they later added a metal filter over the tube which did not permit the emergence of the cathode beam and served as the anode or target. The thin copper filter or transmission anode was plane, planoconvex, or planoconcave to modify the shape and focal sharpness of the emergent beam. Chaoul, of the

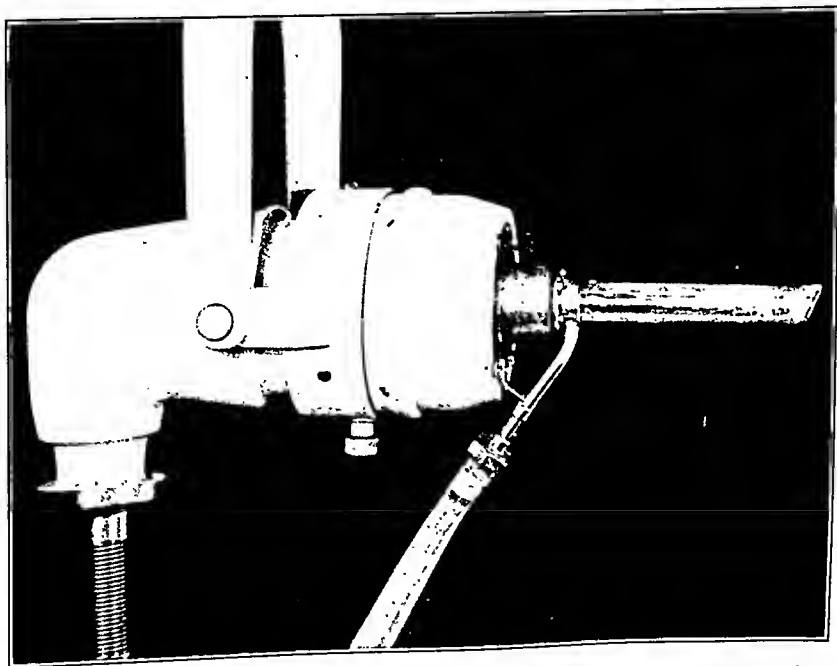


Fig. 13.—Chaoul low voltage contact x-ray tube with tube holder. The target is in the extreme tip of the narrow cylinder. The attached rubber tubes at the base of the cylinder are for the water-cooling system. The unit is about the size of the average dental radiographic outfit, yet is capable of intensive and effective low voltage x-ray therapy.

Charité Surgical Clinic, Berlin, designed a similar apparatus for low voltage, short-distance, or contact x-ray therapy, which was limited to a voltage range of 50 to 60 kv. with a filtration of 0.2 mm. of copper. The anode is so placed that the tube operates at contact or 3 to 5 cm. target skin distance. (Fig. 13.) It has applicators or cones of various sizes and shapes to place against the cancers to be treated. The Chaoul machine is water cooled and shockproof.

The short-distance or contact x-ray treatments make possible the delivery of doses to the tumor sufficient to disintegrate tumor cells and yet spare the healthy surrounding tumor bed by using small fields

sharply localized about the tumor. It furnishes limitation of depth effect by producing a steep energy gradient. The latter is obtained by decreasing the target skin distance and the voltage delivered to the tube. With this apparatus, a soft x-ray beam is utilized and these rays are absorbed in the superficial tissues. For contact application, the dosage rate is approximately 800 r. units per minute; for a target skin distance of 3 cm., it is approximately 88 r. units per minute; and for a target skin distance of 5 cm., it is approximately 36 r. units per minute. This apparatus, of course, has only a specialized usefulness for the treatment of superficial tumors of the hands and feet. Because the depth dose is not great, and the major portion of the radiant energy is absorbed by the tumor proper, the deeper structures

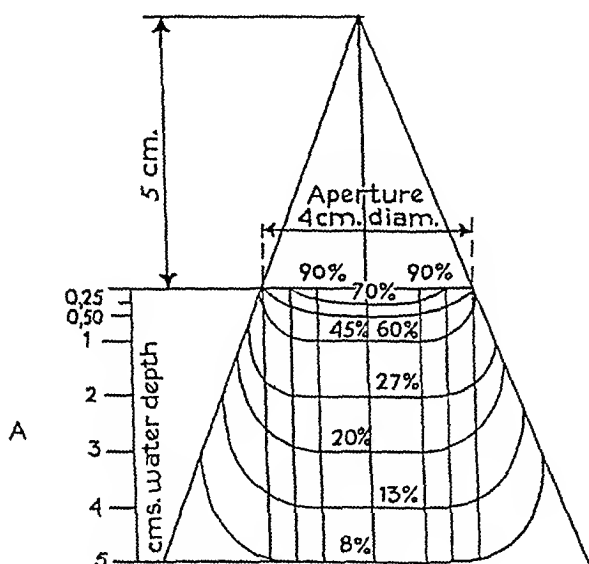


Fig. 14.—Isodose chart with 5 cm. F.S.D., 60 kv.; filter 0.2 mm. Cu; aperture of applicator, 4 cm. diameter.

of the hands and feet are uninjured and the hazards of late radiation necrosis are considerably lessened. The reaction is sharply circumscribed around the cancer. For epitheliomas of the hands and feet, we have used daily fractions of 250 to 400 r. units with total dosages ranging anywhere from 3,000 to 8,000 r. units, depending on the dimensions and radiosensitivity of the cancer. (Fig. 14.)

*Philips Contact Roentgen Therapy.*—A more flexible and equally serviceable unit has been designed by Philips (Fig. 15). This complete outfit is contained in a small portable cabinet, mounted on casters and weighing 325 pounds. It can be used in any room that contains an outlet for 110 volt alternating current. The high tension transformers, the filament transformers for the tube and the valve, the condenser, the blower which supplies the air for the cooling of the tube, and all

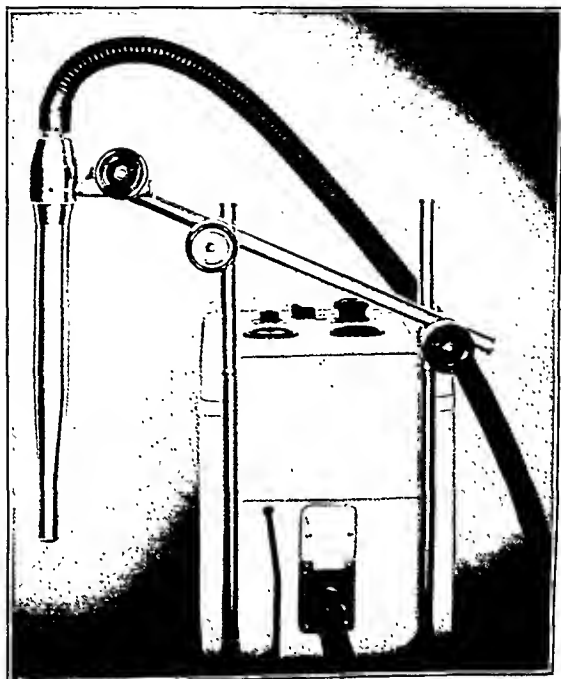


Fig. 15.—Phillips low voltage contact x-ray outfit. The aircooled x-ray tube is within the long proboscis-like cylinder. The target is at the extreme end of this tube. The handle may be disengaged from the standard and held with the hands while treatment is in progress. The rubber-covered cable, 2 M. in length, permits great flexibility.

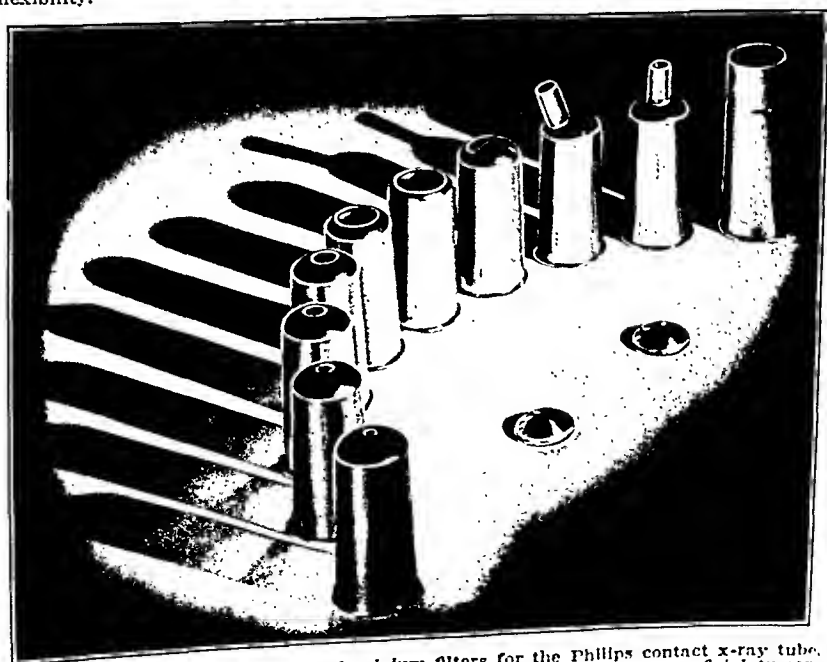


Fig. 16.—Cones and additional aluminum filters for the Phillips contact x-ray tube. These cones provide outlets of different shapes and dimensions for superficial tumors and precancerous lesions.

other component parts except the tube itself are contained within the compact cabinet. A shockproof flexible cable, 2 M. in length, connects the tube to the unit. The x-ray tube is shockproof and is unipolar, the cathode side being grounded. As in the Chaoul machine, the x-rays emerge axially. The cooling air passes through the hose arranged around the shockproof cable and leaves the tube by orifices provided on the tube.

The inherent filter of the tube and shockproof shield is the equivalent of only 0.2 mm. Al. If additional filtration is deemed necessary, disks of 1 or 2.5 mm. Al thickness may be inserted over the tube end and held in place by attached treatment cones (Fig. 16).

The diameter of the emergent x-ray beam is slightly less than 2 inches, therefore the fields to be irradiated must be necessarily small. If tumors of greater surface area are to be treated, as frequently occurs for epitheliomas and hemangiomas, the lesions are subdivided into multiple fields or ports.

The distance of the focus from the target to the protection cap over the tube end is 18 mm. Over this tube end is placed a localizing cone which increases the inherent target contact distance to 2 cm. The intensity is always at 50 kv. constant potential. Two milliamperes is the current employed, although the tube is capable of functioning with 3 Ma. if the time of treatment is short.

TABLE XIV  
PHILIPS CONTACT X-RAY TUBE (50 KV.—2 MA.)

DOSE IN R.	TIME IN SECONDS (") OR MINUTES (')		
	0.0 MM. AL	1.0 MM. AL	2.5 MM. AL
<i>T.S.D.</i>			
<i>Contact (20 Mm.)</i>			
500	3½"	13"	38"
1,000	7"	27"	1' 16"
1,500	10"	41"	1' 54"
2,000	14"	55"	2' 32"
2,500	17"	1' 8"	3' 10"
3,000	21"	1' 22"	3' 48"
r./min.	8,700	2,200	790
DOSE IN R.	TIME IN MINUTES (') OR SECONDS (")		
	0.0 MM. AL	1.0 MM. AL	2.5 MM. AL
<i>T.S.D.</i>			
<i>2 Cm. From Surface (40 Mm.)</i>			
500	13"	1' 8"	2' 42"
1,000	27"	2' 16"	5' 25"
1,500	40"	3' 23"	8' 7"
2,000	53"	4' 33"	10' 48"
2,500	1' 6"	5' 41"	13' 31"
3,000	1' 20"	6' 49"	17' 14"
r./min.	2,250	440	185

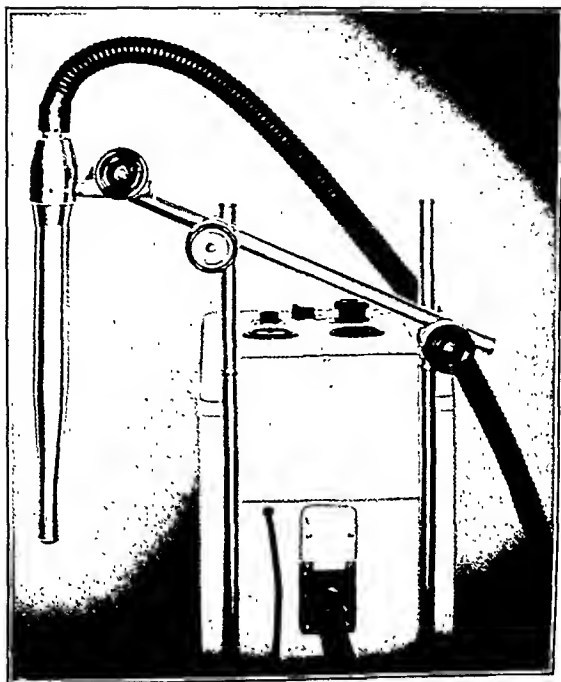


Fig. 15.—Philips low voltage contact x-ray outfit. The aircooled x-ray tube is within the long proboscis-like cylinder. The target is at the extreme end of this tube. The handle may be disengaged from the standard and held with the hands while treatment is in progress. The rubber-covered cable, 2 M. in length, permits great flexibility.

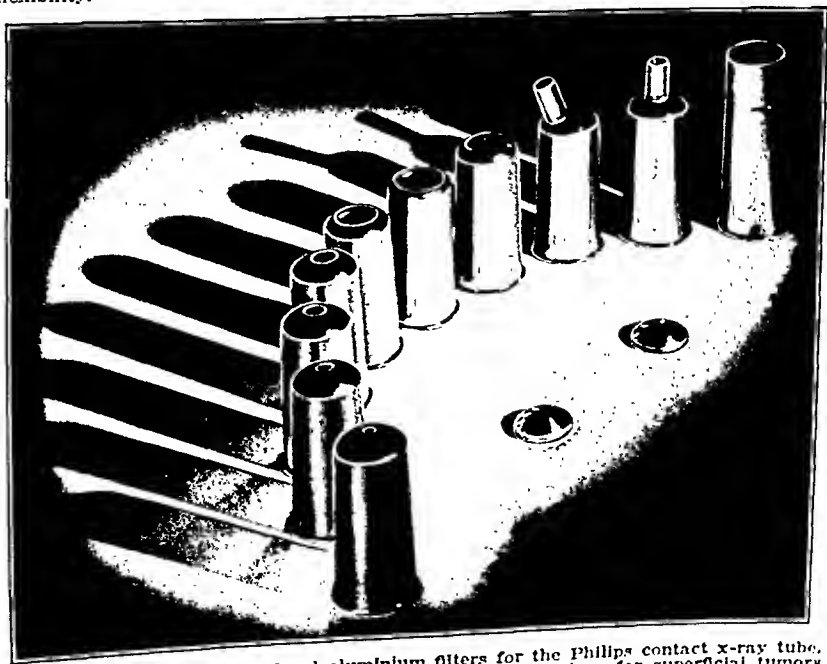


Fig. 16.—Cones and additional aluminum filters for the Philips contact x-ray tube. These cones provide outlets of different shapes and dimensions for superficial tumors and precancerous lesions.

## CARCINOMA OF THE HANDS AND FEET

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ALTHOUGH carcinoma vies with fibrosarcoma in being the most frequently occurring malignant tumor of the soft tissues of the extremities, its incidence is not great and only some 5 to 10 per cent of cutaneous carcinomas occur on the hand and foot (Desaive, De Asis, DeBell, Stevenson, Geschickter, Koehler, Knowles, and Sigel).

The upper extremity is affected two to three times as frequently as the lower, an incidence which argues for the importance of trauma as a factor, although the nature of the irritative agent is not always clear. The chronic irritation which leads to calluses on the hands and corns on the feet never produces carcinoma nor is carcinoma prone to occur on the basis of a varicose ulcer; in fact, its occurrence there is of the greatest rarity.

Carcinomas of the extremities may be classified into three large groups, according to apparent etiologic factors. This subdivision must be arbitrary since the actual significance of any of the assumed etiologic factors is unknown. A convenient grouping is as follows:\*

- I. Carcinomas arising in connection with trauma or irritation
  - a. Irradiation
    - X-ray
    - Radium
    - Solar (such as exemplified by senile keratoses, keratoses in sailors, farmers, etc.)
  - b. Chemical irritation, external (e.g., tar, anilin, pitch, etc.)  
Internal (arsenic)
  - c. Chronic mechanical irritation
  - d. Scar tissue irritation (burn scar especially)
  - e. Irritation from a single trauma or chronic infection, syphilitic ulcer, varicose ulcer, etc.
- II. Carcinoma arising in some previous skin tumor
- III. Carcinoma arising from normal skin

*X-Ray and Radium Dermatitis and Carcinoma.*—Oudin in 1897 recognized that dermatitis and epithelioma may follow exposure to roentgen irradiation, but his early warning was not seriously taken, and as a result the medical profession has furnished and still is furnishing

\*Received for publication, May 25, 1928.

\*Adair, in describing briefly the various types of epitheliomas of the hand, has classified them into six groups, those occurring: (1) in the aged, (2) as result of exposure to the elements, (3) in burn scars, (4) subsequent to internal medication, (5) following chemical irritation, and (6) following x-rays and radium irradiation.



The actual tube is within a long, light, metal cylinder which is handled at will by means of an attached grip. It may be held by the hands during treatment, or, if a long treatment is planned, the tube may be supported by standards attached to the unit.

The indications are the same as those mentioned for the Chaoul machine. There is a distinct advantage, however, in the roentgen output of the Philips tube, which is so great that only a very short time is necessary to complete any treatment. The total dose administered for skin tumors of the hands and feet varies from 1,500 r. units for hemangiomas to 8,000 r. units (2 cm. distance) for epitheliomas.

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ALTHOUGH carcinoma vies with fibrosarcoma in being the most frequently occurring malignant tumor of the soft tissues of the extremities, its incidence is not great and only some 5 to 10 per cent of cutaneous carcinomas occur on the hand and foot (Desaive, De Asis, DeBell, Stevenson, Geschickter, Koehler, Knowles, and Sigel).

The upper extremity is affected two to three times as frequently as the lower, an incidence which argues for the importance of trauma as a factor, although the nature of the irritative agent is not always clear. The chronic irritation which leads to calluses on the hands and corns on the feet never produces carcinoma nor is carcinoma prone to occur on the basis of a varicose ulcer; in fact, its occurrence there is of the greatest rarity.

Carcinomas of the extremities may be classified into three large groups, according to apparent etiologic factors. This subdivision must be arbitrary since the actual significance of any of the assumed etiologic factors is unknown. A convenient grouping is as follows:\*

- I. Carcinomas arising in connection with trauma or irritation
  - a. Irradiation
    - X-ray
    - Radium
    - Solar (such as exemplified by senile keratoses, keratoses in sailors, farmers, etc.)
  - b. Chemical irritation, external (e.g., tar, anilin, pitch, etc.)  
Internal (arsenic)
  - c. Chronic mechanical irritation
  - d. Scar tissue irritation (burn scar especially)
  - e. Irritation from a single trauma or chronic infection, syphilitic ulcer, varicose ulcer, etc.
- II. Carcinoma arising in some previous skin tumor
- III. Carcinoma arising from normal skin

*X-Ray and Radium Dermatitis and Carcinoma.*—Owldin in 1897 recognized that dermatitis and epithelioma may follow exposure to roentgen irradiation, but his early warning was not seriously taken, and as a result the medical profession has furnished and still is furnishing

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\*Adair, in describing briefly the various types of epitheliomas of the hand, has classified them into six groups, those occurring: (1) in the aged, (2) as result of exposure to the elements, (3) in burn scars, (4) subsequent to internal medication, (5) following chemical irritation, and (6) following x-rays and radium irradiation.

The actual tube is within a long, light, metal cylinder which is handled at will by means of an attached grip. It may be held by the hands during treatment, or, if a long treatment is planned, the tube may be supported by standards attached to the unit.

The indications are the same as those mentioned for the Chaoul machine. There is a distinct advantage, however, in the roentgen output of the Philips tube, which is so great that only a very short time is necessary to complete any treatment. The total dose administered for skin tumors of the hands and feet varies from 1,500 r. units for hemangiomas to 8,000 r. units (2 cm. distance) for epitheliomas.

stance, particularly in the walls of the blood vessels, became thick and swollen and was later replaced by fibrous tissue (Fig. 1C). Flaskamp, along with Rost, believes that the rays attack the cells directly and that the effect which is most felt in the nucleus is noted also in the cytoplasm. Because of the spottiness of the injury, repair may occur, provided of course repeated damage is not done; but with continued

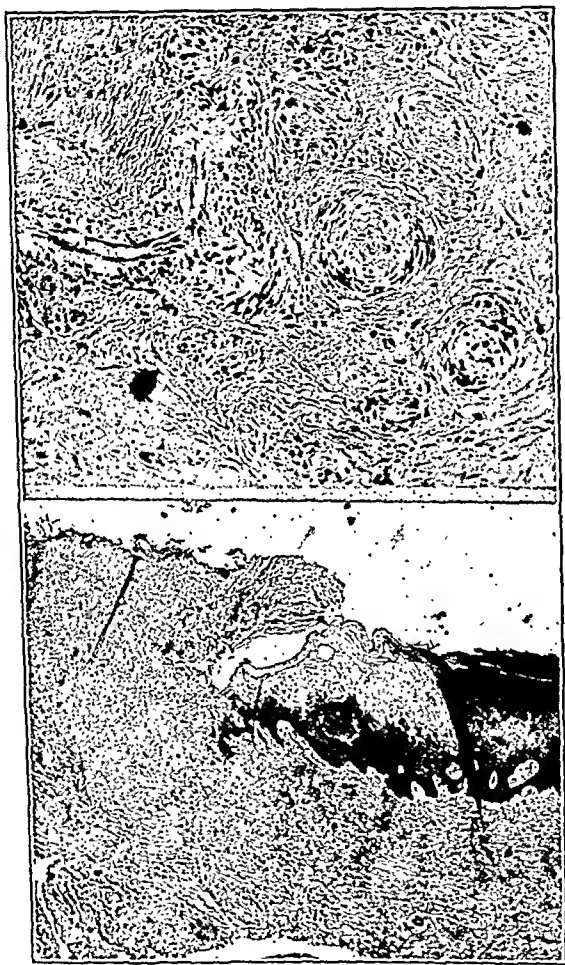
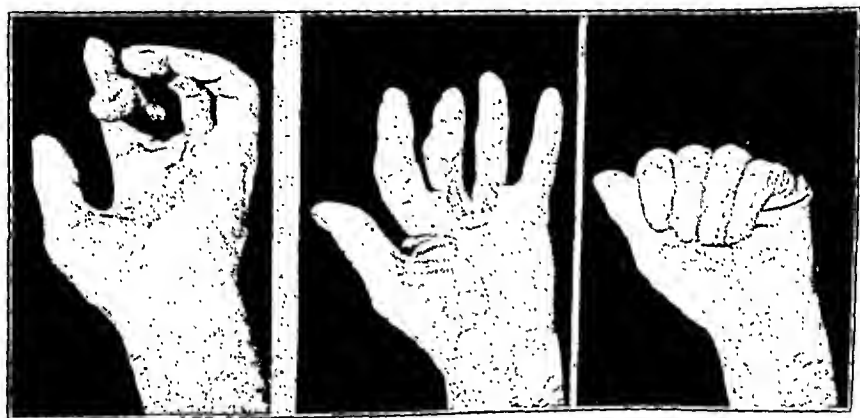


FIG. 1C.—See opposite page for legend.

exposure, the susceptibility of the skin increases and a chronic dermatitis develops. Pullinger has shown experimentally that the effects resemble those of inflammation. There is first a stage of hyperemia, which, if sufficiently severe, is followed by exudation, extravasation of blood, and thrombosis. While her study was not made with reference to chronic irradiation dermatitis, the importance of vascular injury is apparent.

many martyrs to the x-ray. The professional radiologist has learned to protect himself from the cumulative effects of adventitious irradiation incident to manipulation and fluoroscopy. The general practitioner, however, who uses the x-ray incidental to his practice is exposed to minute doses of irradiation over a long period of time. The great majority of patients presenting themselves for treatment of irradiation dermatitis and carcinoma are practicing physicians and surgeons and not professional roentgenologists. (Figs. 1-3.)

The chronic irradiation dermatitis which subsequently exhibits carcinomatous changes must be distinguished from the acute dermatitis which follows excessive exposure over a short period of time. The acute dermatitis may produce painful ulceration and weeks or months may be required to bring about healing; rarely however does carcinoma develop in it.

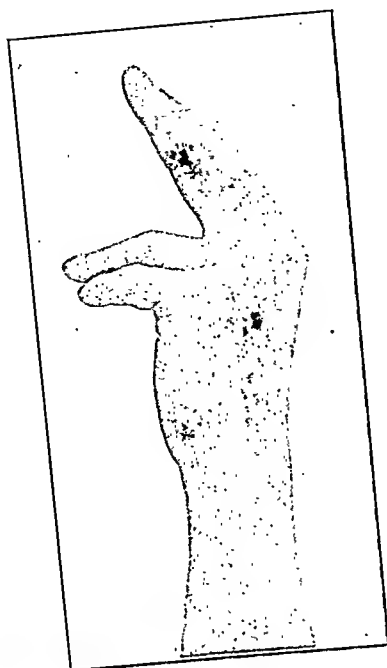


A.

B.

Fig. 1.—A, Precancerous hyperplasia of hand due to irradiation (P.M.H. 8114, 1931). Thirty years previous to admission to hospital the patient, a 69-year-old doctor, began to use the x-rays in examination of patients. Shortly afterwards a dermatitis developed and later a few areas of keratosis which were removed with radium. The skin remained rough and inflamed, but no serious trouble developed until 1929 (almost twenty-eight years after the onset) when a fissure, the size of a navy bean, appeared between the ring and middle fingers. The fissure persisted without symptoms for a year, at which time radium was applied and the fissure disappeared for a month. A recurrence of the ulcer was treated again with radium and this time the ulceration became larger and very painful and a second ulcer developed in the palm. These ulcers were excised and the raw area covered with a split graft in October, 1931. Healing occurred and there was no recurrence of the condition at the time of death from some other cause some twenty months later. B, Condition of hand five months after application of split graft. C, Photomicrographs of the tissues removed from the patient shown in A, showing the endarteritis and fibrosis of the subcutaneous tissues and the inflammatory hyperplasia (precancerous) of the skin at the margin of the ulcer.

The manner in which irradiation leads to the peculiar changes in the skin and subcutaneous tissues which lead up to keratosis, ulceration, and finally carcinoma is a matter of controversy. It is not known whether there is a direct action of the rays upon the skin or whether irradiation produces its effects through the intermedium of some chemical substance released by the rays. Porter and Wolbach believed that the rays had an especial affinity for collagen and that this sub-



A.



B.

C.

Fig. 3.—A. Roentgen dermatitis and carcinoma with history extending over a period of twenty-eight years. Hyperkeratosis had started fifteen years previously following x-ray irradiation, and one year previously (1921) an ulcer had developed on the middle finger, numerous areas of hyperkeratosis over the dorsum of the hand, and an enlarged axillary node. The finger was amputated and the axilla was dissected; carcinoma was found in both places. B. Photomicrograph of the squamous cell carcinoma of the middle finger. C. Photomicrograph of the carcinoma metastasis in an axillary node.

The dermatitis and carcinoma which follow repeated minimal adventitious exposures to x-rays are characterized by latency and multiplicity (Figs. 1-3). The dermatitis does not develop immediately after the initial exposures, but months or even years may elapse before the keratoses and telangiectases appear. They do not necessarily become malignant, and, if exposure is avoided not only to roentgen and radium irradiation but to excessive sunlight and possibly even to irritant chemicals as well, the lesions may remain stationary and the hands may be kept fairly comfortable by the use of bland creams. Usually, however, once started the keratosis and dyskeratosis do not disappear and new areas develop in previously normal appearing skin. Then,

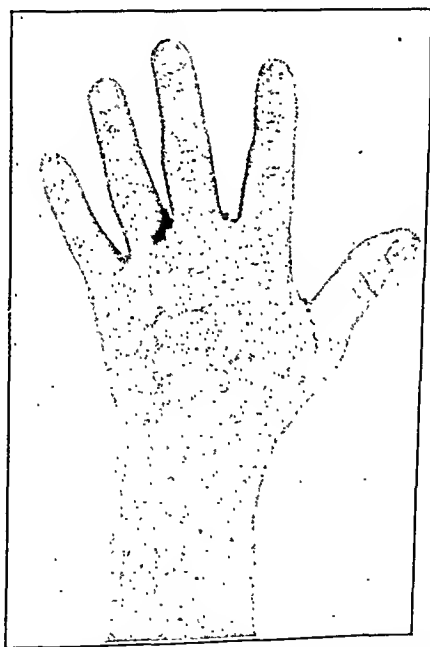
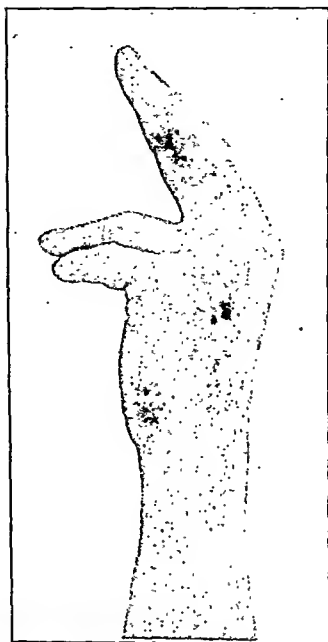


Fig. 2.—Early epidermoid carcinoma on dorsum of left hand in a 52-year-old physician. (P.M.H. 14703, 1933.) In 1918 the hand was exposed to a considerable dose of x-ray irradiation and a few months later an ulcer developed, which persisted without pain or increase in size for five years, at which time the hand became quite sealy. Both the ulcer and the sealiness have remained unchanged for some thirteen years. The ulcer was excised, a free full-thickness graft applied, and healing occurred without reaction. Microscopic study of the ulcer showed considerable inflammatory hyperplasia of the skin, irregular branching masses of epithelial cells with numerous mitoses, and marked diminution of vascular supply.

especially if further exposure takes place or if unwise treatment is given, changes occur which we recognize as cancerous or as precancerous. There appear painful cracks or ulcers which become infected and heal with great difficulty. Some may never heal or the same area may repeatedly break down, finally to form a progressively enlarging persistent ulcer. Such an ulcer may prove to be a carcinoma, but it rarely recurs following excision. However, a succession of such keratotic areas may break down, ulcerate, and become malignant, and it



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B.

C.

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is this chronicity and the multiplicity of malignant lesions which characterize irradiation dermatitis and give the clue to treatment.

The tendency in the treatment of irradiation carcinoma is frequently too conservative in that, while the ulcerating lesions are removed, large areas of keratotic skin are left behind. It should be remembered that the damage is extensively scattered over the dorsum of the hand and fingers, that not one lesion but from two to twenty or more may develop into carcinoma, and that malignancies developing subsequent to excision are not recurrences but new lesions. All damaged skin should be removed, preferably in one stage regardless of the extent of the actually malignant area (Figs. 3E and 3K). Tiny keratoses often may be individually excised or desiccated, and where there are



Fig. 3D.—The patient returned in 1931 for treatment of numerous areas of keratosis and ulceration of the same hand.

but few such areas and considerable normal appearing intervening skin individual removal may be satisfactory. If the disease is extensive, it is necessary to remove practically all of the skin from the dorsum of the hand and fingers.

The removal of a large amount of skin from the hand entails the covering of the raw surface. Some surgeons have advocated a delayed skin graft, preferring to allow the raw surface to become covered with clean granulations before applying a graft. It is my feeling, however, that an immediate graft can be applied if sufficient pains have been taken beforehand to clean the skin and minimize the always present infection. It is our practice to hospitalize the patient for several days or a week preceding operation and during this time, by

frequent changes of dressings and scrupulous cleanliness, to reduce the infection and contamination of the surface.

There is some choice as to the type of graft to be used, depending on the area to be covered and the nature of the raw surface. Following removal of small areas of skin where there is no infection and where tendons are not exposed, a free full thickness graft may be applied. For larger areas the graft of intermediate thickness of Blair and Brown is very useful (Fig. 1). In instances in which sub-

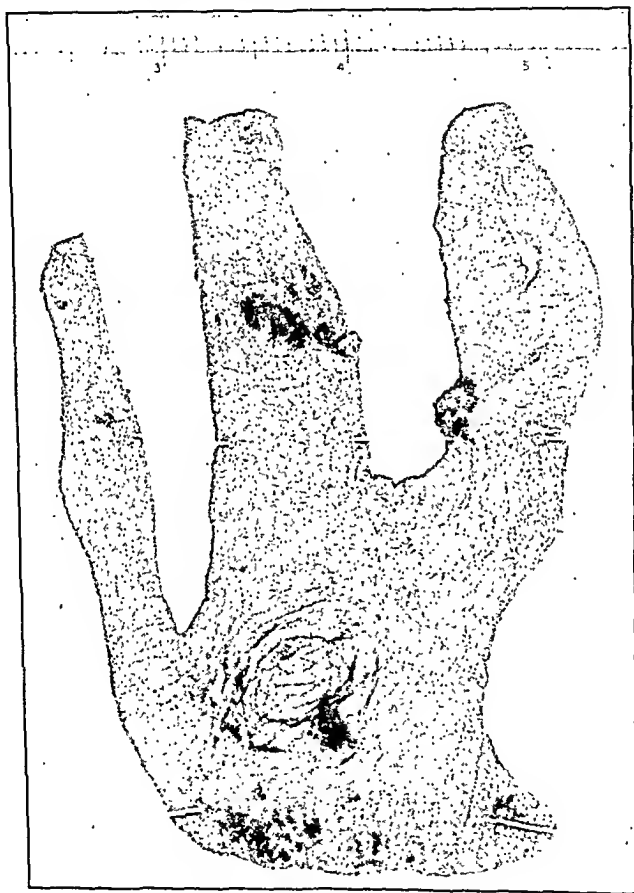


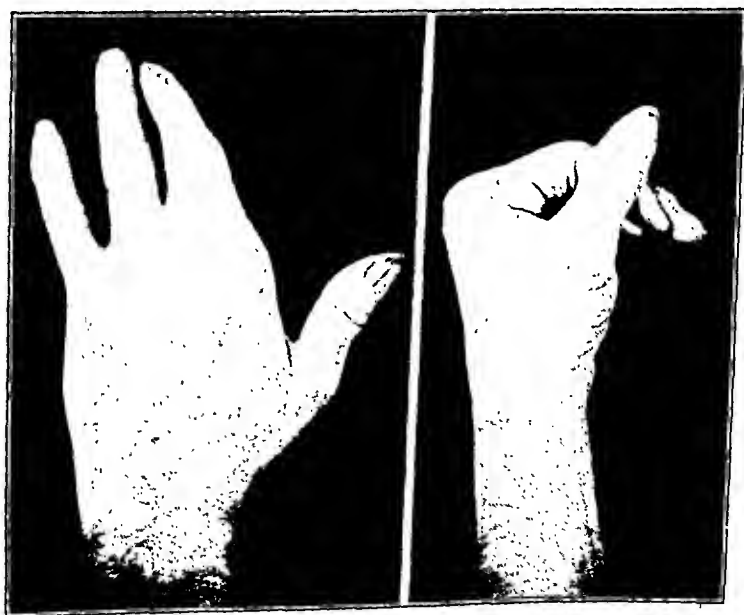
Fig. 3E.—Because of the extensive involvement, the skin over the dorsum was excised in toto.

cutaneous fat is needed, a pedunculated flap or pocket flap is indicated (Fig. 3F).

There is some difference of opinion as to the logical management of the regional lymph nodes. Handley advises radical removal of the epitrochlear and axillary nodes in every case of roentgen carcinoma, regardless of the extent. He also excises the strip of fascia which lies over the medial intermuscular septum and contains the important lymphatic vessels connecting the two groups of nodes, and he states



F.



G.

Fig. 3.—*F*, The hand was placed in a pocket flap on the thigh, where it remained for one month. *G*, The flap healed satisfactorily and in November, 1930, the patient had regained good use of the hand. (In 1934 following exposure on a hunting trip the flap broke down along the radial border on the index finger and this was excised and a small pedunculated flap applied.)



Fig. 3.—*H*, In June, 1930, areas of keratosis excised from the right hand showed beginning basal cell carcinomas. *I*, In August, 1931, a warty growth excised from the left forearm showed early epidermoid carcinoma. *J*, In June, 1931, the patient returned for further treatment of persistent areas of hyperkeratosis on the dorsal surfaces of the fingers of the right hand.

that this operation is a safeguard in case carcinoma develops in subsequent lesions. Blair believes that gland dissection should be performed if the lesion is deep. It is my feeling that in the case of superficial lesions without palpable nodes in which excision of the skin is all that is necessary to remove the diseased areas the glands may be left alone. If, however, it is necessary to amputate fingers, if the lesion has penetrated into the deep fascial planes, tendons, or bones, if palpable nodes are present, an axillary and epitrochlear dissection should be carried out.

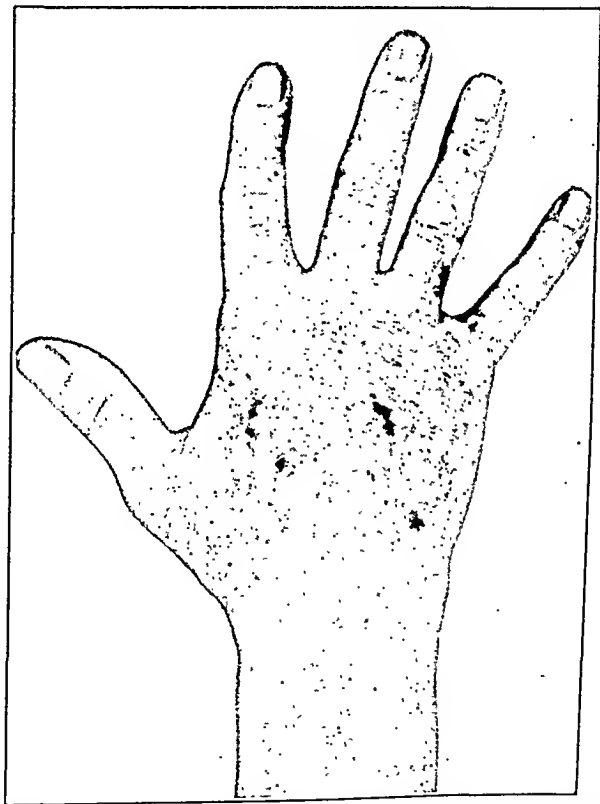


Fig. 3K.—These areas were all excised and microscopic examination revealed marked inflammatory hyperplasia of the skin, the so-called precancerous stage.

The use of any type of irradiation is absolutely contraindicated. Even the mild exposure to ultra-violet irradiation which is sustained on a golf course may occasion great discomfort to a patient with an "x-ray hand." It would hardly seem necessary to caution against the use of radium or x-ray were it not that these agents are so frequently employed. In the early stages of the dermatitis before the real nature of the lesion is recognized, irradiation, while possibly excusable, may lead to serious trouble. There is no justification how-

ever for roentgen or radium therapy after the true nature of the condition is known.

The prognosis of roentgen carcinoma depends upon the stage it has reached before operative care is given; although they are squamous cell carcinomas, they tend to develop slowly, metastasize late, and there is adequate time for complete eradication. Too often, however, temporizing procedures are tried; there is further exposure to x-rays, and new lesions develop from time to time in regions of the hand not at first seriously involved. If it is remembered that all of the dry keratotic skin on the dorsum of hand and fingers is potentially malignant, wider excisions will be done and fewer recurrences and metastases will occur. The prognosis is not necessarily unfavorable even if the glands are invaded, though admittedly it is not so good. In the case illustrated in Fig. 3 despite axillary metastasis and the subsequent development of other areas of carcinoma on the hand the process did not become generalized, even after some thirteen years.

Carcinoma also may develop on the basis of radium dermatitis but by no means so frequently as in roentgen dermatitis, possibly because radium was introduced later than x-ray and its dangers were realized. I have seen several instances of radium dermatitis, but I have never seen a carcinoma on the basis of chronic radium dermatitis. Such cases have been reported (Wakeley, 1927) and the pathogenesis and pathologic picture appear to be the same as for roentgen carcinoma.

*Solar irradiation* probably plays an important role in the development of carcinoma of the dorsum of the hand in sailors, farmers, and others whose hands are exposed to wind and weather for long periods of time. The keratoses which appear in old people are also probably the result of these same influences and it is not always certain how much significance is to be attached to the different types of irritation, sun, wind, mechanical irritants, and the lowered vitality of aged skin. The irritating property of sunlight to skins already afflicted with roentgen dermatitis is well recognized.

*Carcinoma of the extremities following exposure to chemicals* is found chiefly on the hands of persons exposed to tar, grease, gasoline, oil, and paint. Adair believes this type of occupational carcinoma is on the increase, that service station employees are especially liable to develop it, and that the danger is especially great in the case of a combination of chemical and mechanical trauma. Ligge, who has studied the problem of occupational dermatitis and carcinoma in industry in Great Britain, has found that workers exposed to pitch, tar, paraffin, mineral oil, and their derivatives show a high incidence of cutaneous carcinoma. Briquette workers and cotton-mule spinners develop carcinoma as the result of exposure of the skin to irritant chemical oils, especially certain types of mineral oil. Ligge found in 123 cases of carcinoma among briquette workers 9 involving the hand; and of

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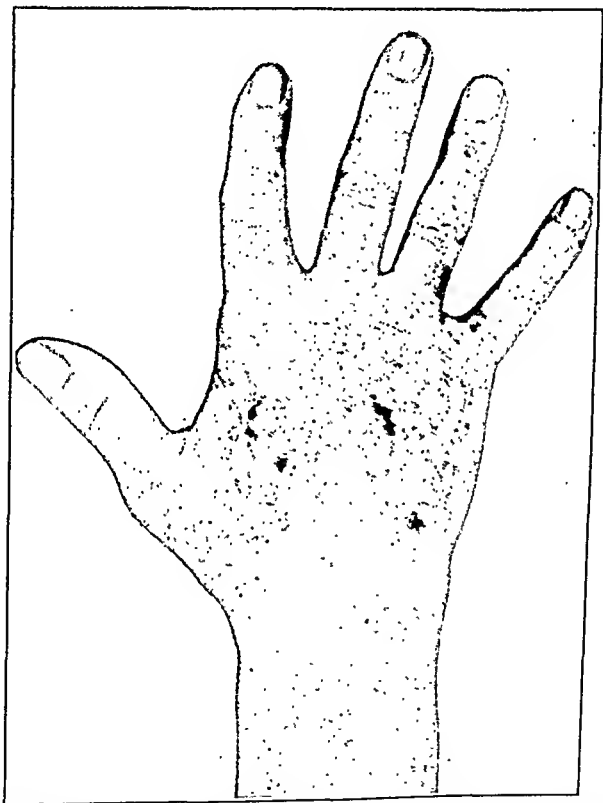


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which it lies. There are some who believe that the carcinoma develops from epithelial cells which have been displaced and lie in the connective tissues of the scar. These cells following nutritional disturbance and trauma are thought to be the ones which undergo carcinomatous proliferation.

*The active lupus lesion or the lupus scar* appears to be a site for the development of carcinoma with sufficient frequency that the lupus carcinoma has come to be a clinical entity. According to Mündelein's statistics, 3.2 per cent of all cases of lupus develop carcinoma. In 2,575 cases he found 83 with carcinoma; of these 5 occurred on the extremities, 4 on the upper and 1 on the lower. There is no agreement as to the factors leading to the development of carcinoma in lupus. The lupus itself, the long-continued epithelial proliferation which it produces, and the constant irritation of medicaments used in treatment have been suggested as possibilities. Roentgen irradiation has been accorded a prominent place and some have suggested that since the advent of roentgen treatment lupus carcinoma has increased. This assertion, however, has not been definitely proved (Mündelein).

*Other types of chronic inflammatory processes* may lead to the development of carcinoma. Draining sinuses of various types and chronic nonspecific ulceration may eventually become malignant. Carcinoma may develop in osteomyelitic sinuses; the epithelial proliferation may occur in skin which has grown into the sinus from the surface; and the bone may be the seat of a primary epithelial neoplasm and the carcinoma may go unrecognized for a long period of time. Carcinoma develops very rarely in chronic varicose ulcers. Tenopyr and Silverman analyzed 1,000 cases of chronic ulcers of the leg and found but 14 cases of malignancy. Of these, some 4 appeared to have developed on the basis of a varicose ulcer; 5 apparently were primary carcinomas of the skin; 2 were ulcers of less than two years' duration (and were considered primary); 1 occurred in an osteomyelitis wound; 1, in a compound fracture; and 1, in a burn scar. They cite the literature and note especially the work of Knox (1925), who was able to collect 59 instances of carcinoma of the leg, about one-half of which seemed to have developed on the basis of ulcer. Chronic paronychia (Silverman) is occasionally the basis for the development of an epithelioma.

Chronic ulceration and carcinoma sometimes follow a single injury and in such instances it is difficult to decide if the injury or the subsequent infection is the etiologic factor (Fig. 4). Among such single injuries which have preceded the development of carcinoma are various types of puncture wounds, animal bites, and crushing injuries to the nail bed. Duhot, Layne and Delacourt have briefly reported an instance of carcinoma of the hand which followed a puncture wound with copper wire and note six other similar cases in their report. In the present state of our knowledge it is not possible to be dogmatic about the possibility of the development of carcinoma following a



1,062 cases of carcinoma in cotton-mule spinners, who are exposed to mineral oil spray from the spindles, 70 per cent involved the scrotum and 30 per cent the hands, arms, and other parts of the body. The Public Health Bulletin No. 215, in reporting upon the skin hazards in American industry, found 12 cases of carcinoma among 4,507 workers in the oil and wax industry; of these, 2 were on the hand.

Arsenic is the only internal medication which appears to cause carcinoma of the skin. The majority of patients with arsenical dermatitis give a history of having continued the use of Fowler's solution on their own responsibility for many years after it had been prescribed. The first lesions occur typically as patches of hyperkeratosis and scaling on the palms and soles, but as the disease progresses more and more of the body surface is involved until finally most of the skin of the body is affected. Malignancy may develop in any of the cutaneous lesions and makes itself manifest by the appearance of cracks and ulceration in areas of keratosis. Pain seems to be a rather typical feature of this carcinoma. In common with irradiation carcinoma malignancy may occur in more than one of the areas of arsenical keratosis. The prognosis is bad probably because the chronic nature of the lesions leads to neglect in seeking treatment and because of the development of multiple malignancies.

*Chronic mechanical trauma* does not appear to be very frequently the cause of carcinoma of the extremities. Although Volkmann recorded one case developing on the basis of an ingrown toenail, the case appears to be unique despite the great frequency of this supposedly causative factor. Most reports of cases of carcinoma ascribed to mechanical trauma consist of single case records. The rarity of carcinoma in corns and calluses minimizes the importance of chronic mechanical trauma, certainly when acting alone.

*Carcinoma may occur in cutaneous scars*, particularly those resulting from burns (Treves and Pack), the "Marjolin ulcer." The burn scar is the most frequent single definite factor in the development of carcinoma of the extremities. A striking characteristic of the burn scar is the long duration before carcinoma develops. In a collected series of burn scar carcinomas of the hand the average duration of the scar before the onset of malignancy was found to be 43.3 years, the oldest scar being 66.5 years and the youngest 3 months. The factors which lead to the occurrence of carcinoma in a burn scar are not clearly understood; in fact, there are some who doubt the validity of the term "burn scar carcinoma." However, it occurs with sufficient frequency and is present so often in carcinoma of the extremities that it must be seriously considered. The factors in burn scar which appear to predispose to the development of cutaneous carcinoma are probably two: vascular and traumatic. The thin skin which covers the thick avascular fibrous scar is poorly nourished and easily traumatized, both because of its elevated position and the thick hard tissue over

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Chronic ulceration and carcinoma sometimes follow a single injury and in such instances it is difficult to decide if the injury or the subsequent infection is the etiologic factor (Fig. 4). Among such single injuries which have preceded the development of carcinoma are various types of puncture wounds, animal bites, and crushing injuries to the nail bed. Duhot, Layne and Delacourt have briefly reported an instance of carcinoma of the hand which followed a puncture wound with copper wire and note six other similar cases in their report. In the present state of our knowledge it is not possible to be dogmatic about the possibility of the development of carcinoma following a

1,062 cases of carcinoma in cotton-mule spinners, who are exposed to mineral oil spray from the spindles, 70 per cent involved the scrotum and 30 per cent the hands, arms, and other parts of the body. The Public Health Bulletin No. 215, in reporting upon the skin hazards in American industry, found 12 cases of carcinoma among 4,507 workers in the oil and wax industry; of these, 2 were on the hand.

Arsenic is the only internal medication which appears to cause carcinoma of the skin. The majority of patients with arsenical dermatitis give a history of having continued the use of Fowler's solution on their own responsibility for many years after it had been prescribed. The first lesions occur typically as patches of hyperkeratosis and scaling on the palms and soles, but as the disease progresses more and more of the body surface is involved until finally most of the skin of the body is affected. Malignancy may develop in any of the cutaneous lesions and makes itself manifest by the appearance of cracks and ulceration in areas of keratosis. Pain seems to be a rather typical feature of this carcinoma. In common with irradiation carcinoma malignancy may occur in more than one of the areas of arsenical keratosis. The prognosis is bad probably because the chronic nature of the lesions leads to neglect in seeking treatment and because of the development of multiple malignancies.

*Chronic mechanical trauma* does not appear to be very frequently the cause of carcinoma of the extremities. Although Volkmann recorded one case developing on the basis of an ingrown toenail, the case appears to be unique despite the great frequency of this supposedly causative factor. Most reports of cases of carcinoma ascribed to mechanical trauma consist of single case records. The rarity of carcinoma in corns and calluses minimizes the importance of chronic mechanical trauma, certainly when acting alone.

*Carcinoma may occur in cutaneous scars*, particularly those resulting from burns (Treves and Pack), the "Marjolin ulcer." The burn scar is the most frequent single definite factor in the development of carcinoma of the extremities. A striking characteristic of the burn scar is the long duration before carcinoma develops. In a collected series of burn scar carcinomas of the hand the average duration of the scar before the onset of malignancy was found to be 43.3 years, the oldest scar being 66.5 years and the youngest 3 months. The factors which lead to the occurrence of carcinoma in a burn scar are not clearly understood; in fact, there are some who doubt the validity of the term "burn scar carcinoma." However, it occurs with sufficient frequency and is present so often in carcinoma of the extremities that it must be seriously considered. The factors in burn scar which appear to predispose to the development of cutaneous carcinoma are probably two: vascular and traumatic. The thin skin which covers the thick avascular fibrous scar is poorly nourished and easily traumatized, both because of its elevated position and the thick hard tissue over

that some benign neoplasm has undergone so-called malignant degeneration, the fact remains that this group of carcinomas is the most malignant of all of those of the hand.

Occasionally the skin has been normal until the neoplasm developed; there is no history of any irritation, no scar or chronic infection, irradiation or previous neoplasm.

A few general etiologic factors are of some interest. The average age of 239 cases of carcinoma of the hand was found to be 59 years, with practically the same average for each sex. It does not appear to hold true that carcinoma of the hand develops at a more youthful age when it occurs in a congenital neoplasm than when some irritative factor is present.

Males outnumber females almost 2 to 1 and in the chronic irritation group slightly over 2 to 1; whereas, the roentgen carcinoma occurs almost exclusively in males. Carcinoma of the hand is often spoken of as carcinoma of the dorsum because of its most frequent location. Except in the case of roentgen carcinoma, the right side is more often attacked than the left in a ratio of slightly less than 2 to 1. However, of those cases in which the tumor developed from apparently normal skin, the ratio in 25 cases was 12 right to 13 left.

Carcinomas of the hand are usually characterized by a long chronic course. As a rule an ulcer has been present for from one or two years before the condition is diagnosed as carcinoma and it is logical to assume that it has actually been malignant for most of that time. For convenience of description the clinical course may be divided into the preulcerative and the ulcerative stages. The lesion usually starts as an indurated nodule or as a scaly symptomless tumor, the surface of which may be thin, dry, and parchment-like or hypertrophic with gray or reddish papillary projections from its surface and surrounded by dilated capillaries. Such lesions may persist without causing disturbance for many years and then break down, spontaneously or after trauma. Cracks may appear which refuse to heal or crusts may form which upon being removed leave a thin, red, shiny or ulcerated surface. There then develops an ulcer or an irregular granular cauliflower-like mass.

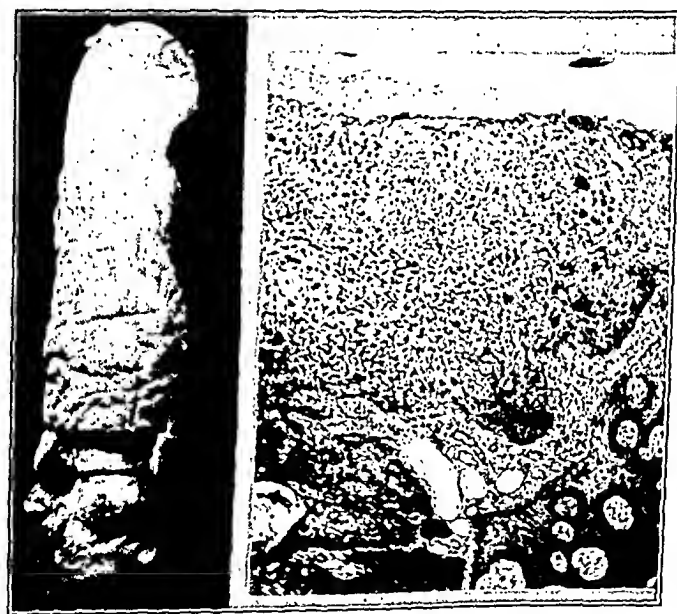
The ulcer or cauliflower growth enlarges slowly, involving first the neighboring skin and subcutaneous tissues. It may attain quite sizable dimensions before the deeper structures are actually invaded. Tendon, bone, and muscles, however, eventually are involved, although this may not occur until quite late. As the tumor develops, it becomes infected and necrotic; a seropurulent or serosanguineous discharge appears, often very malodorous. Occasionally hemorrhage takes place and may be quite severe.

Involvement of the lymph glands comes late, often not for two years or more after the ulceration. Of 122 collected cases in which

single trauma. It has never been experimentally produced and in such cases as are reported the data are often insufficient to warrant a definite conclusion.

Various other lesions (furuncles, carbuncles, and pellagrous dermatitis) have been given as precursors of carcinoma on the hand.

*Carcinoma may develop on the basis of some previous skin tumor and in such instances there is always the question whether the lesion has not been malignant from the start (Higginson). The previously present neoplasms may have been congenital tumors or they may have appeared some time in later life. Carcinomas appearing in congenital neoplasms are quite rare, but their invariably malignant course puts them in a group by themselves.*



A.

B.

Fig. 4.—A, Subungual carcinoma of nail bed, left little finger, which followed a severe crushing injury nine months previously. The wound became badly infected and was treated elsewhere with salves and ointments without success. The finger became extremely painful and the patient applied to the Northwestern University Clinics, where amputation was performed by Dr. Hart. There had been no recurrence one year later. B, Photomicrograph of microscopic section shows a squamous cell carcinoma of the nail bed.

Those carcinomas arising in cutaneous warts and nevi which appear in later life usually present a history of some sort of trauma, either accidental or in attempts at self-treatment (Figs. 5 and 6). Not infrequently a cutaneous wart has been treated by irradiation, salves, and incomplete excision each time with prompt recurrence. Such lesions have a worse prognosis than do tumors originating on an irritative basis only; not so bad, however, as do carcinomas occurring in congenital neoplasms. Whatever our opinion may be concerning the origin of the carcinomas, whether or not it appears logical to assume

parenchymatous organs, especially the lungs and liver, are of late occurrence.

The pathologic picture does not differ from that of carcinoma elsewhere on the skin. The majority on the hand are squamous cell in character, a very few are basal cell, and an occasional one transitional or basal squamous carcinoma. A basal cell epithelioma may become a squamous or basal squamous type, and when a basal cell lesion recurs following treatment this transition frequently will be found to have taken place. If a system of grading is followed, 90 to 95 per cent of the tumors will be found to fall into Groups I and II of Broders' classification (DeBell and Stevenson) and only the rare one in Group III and still more rarely in Group IV.

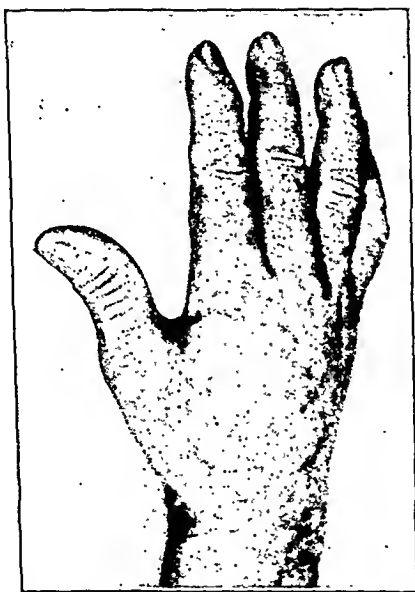


Fig. 6.—Thick split graft applied to surface left by excision of an early squamous cell carcinoma of dorsum of hand (P.M.H. 27107, 1936). The patient, a 72-year-old farmer, noted a wart or pimple on the dorsum of his hand some fifteen to sixteen years previous to admission. The wart came off and a crust formed over the resultant ulcer. For a number of years the ulcer slowly enlarged, crusting over from time to time until finally a purulent discharge developed. The application of various salves and the use of acids did not retard the growth and in 1932-33 eight or ten x-ray treatments were given without benefit. In May, 1934, he was operated upon elsewhere; the area was excised and a skin graft applied. This "took" at first but eventually broke down and the following year ten more x-ray treatments were given. In July, 1936, the ulcer was widely excised by Dr. S. L. Koch and a thick split graft applied. This has remained healed to date.

The diagnosis of carcinoma is made on the gross appearance, substantiated by microscopic sections. The development of malignancy in the brown, dry, scaly keratoses in elderly persons, farmers, sailors, and others exposed to wind, rain, and sun is suggested by induration and a mild inflammatory reaction. In physicians who have been exposed to roentgen irradiation, the presence of hyperkeratoses and ulcers at once suggests the possibility of carcinoma. The exuberant cauliflower-like growths may suggest a granuloma, but cultures and biopsy should make the diagnosis certain. Stubborn lesions of the



information was given, glandular enlargement was present in 62 and absent in 60. The mere presence of enlarged lymph nodes does not connote metastasis since it is often the infection which is accountable. If, however, the nodes are enlarged, they should be considered to be malignant until proved otherwise.

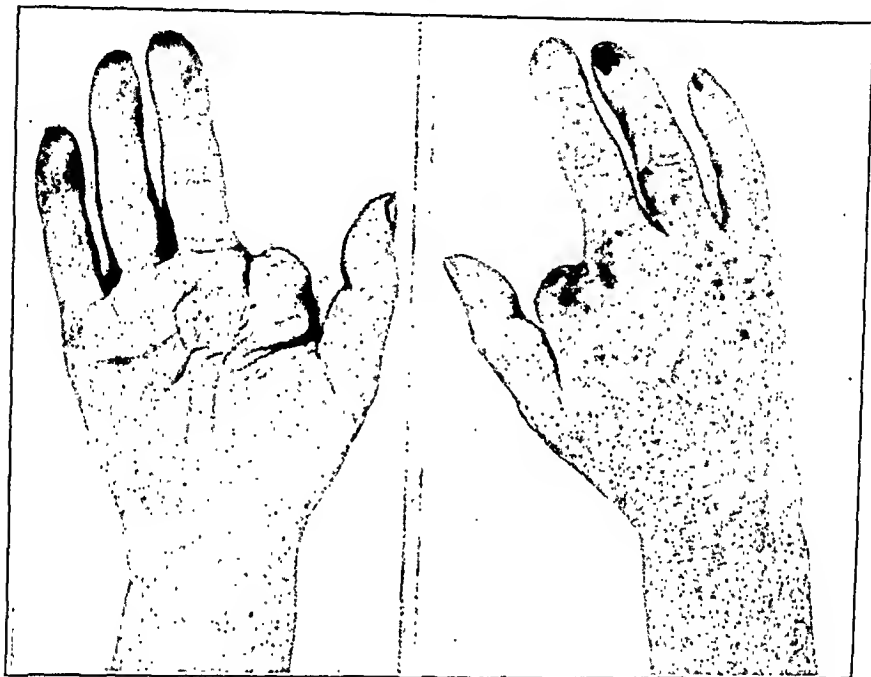


Fig. 5.—(P.M.H. 4771.) Squamous cell carcinomas of right hand in a 42-year-old wool handler. In January, 1934, a small wartlike growth appeared on the dorsum of the distal interphalangeal joint of the index finger. He treated this himself for some six months with sulfuric acid and hot needles without success and finally consulted a physician in June, 1934. There was a most peculiar odor to the discharge at this time and hot borie dressings were applied without results for several weeks. He consulted a second doctor, who snipped off the lesion with scissors and sent the patient to a dermatologist. The small ulcer then present was treated with radium and x-ray, following which a slough developed which left a deep infected ulcer for which the finger was amputated at the proximal interphalangeal joint. The operative wound became infected and a sinus developed between the distal end of the stump and the palm. This was treated as an infection for somewhat over a year, at which time, because of the unbearable pain the patient consulted another surgeon who amputated the stump at the metacarpophalangeal joint. Two months later the pain and swelling recurred and a granulomatous ulcer with a foul-smelling discharge developed in the palm. Biopsy and cultural studies having failed to afford a diagnosis, the patient was given potassium iodide for several months without relief. At time he was first seen, somewhat over two and one-half years after the development of the "wart," the cultures were not significant, but a biopsy revealed an ulcerated squamous cell carcinoma. The hand was amputated through the middle of the forearm in September, 1936, and enlarged axillary lymph nodes dissected out. No metastases were found in the nodes. There has been no recurrence up to December, 1938.

The terminal symptoms are due to the local destructive action of the growth, infection, and occasionally to generalized metastases. Pressure on the brachial plexus by enlarged axillary and cervical nodes may cause excruciating pain which often can be controlled only by nerve section or chordotomy. Toxic absorption or sepsis from the local growth may be overwhelming. Generalized metastases to the

superficial usually may be completely excised and the defect immediately repaired with a graft of intermediate thickness. Here, as in roentgen carcinomas, a careful preparation of the hand is necessary in order to reduce the ever-present surface infection to a minimum. If excision of the tumor has exposed tendon and bone, a pedunculated flap is needed and again the pocket flap will be found to be the most useful.

Although irradiation is extensively used in the treatment of cutaneous carcinoma, it is my feeling that those of the extremity are best treated by excision. The extensive necrosis with exposure and destruction of tendon and bone which are liable to follow therapeutic irradiation of the hand renders it unsuitable in any but the smallest lesions. Burn scar carcinoma, already situated in poorly vascularized tissue, should not be subjected to irradiation.

Deep ulcerating carcinomas and large fungating masses may be so extensive that very mutilating procedures will be needed if local excision is performed. The surgeon must carefully weigh the possibility of sparing a sufficient amount of tissue to leave the patient a functional hand against the possibility of insufficient removal of malignant tissue. Amputation of the extremity occasionally must be practiced, and, because of the ever-present infection both in the local tumor and in the lymphatics of the forearm and arm, primary healing of the stump may not occur. In case of carcinoma of the nail bed it is usually advisable to amputate the digit. These lesions are prone to be very malignant and an occasional one turns out to be a melanoma.

The same procedure with reference to lymph nodes should be followed here as in roentgen carcinoma. If the nodes are not palpable, it is very doubtful if they are invaded; if they are enlarged, the chances are 50 per cent that metastases are present. Enlarged nodes, of course, should be removed, while if the primary lesion is deep and invasive and if amputation is necessary a dissection of the axillary and epitrochlear glands should be practiced.

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nail bed which resemble paronychia may be treated for some time as chronic infections before the true nature of the condition is suspected and proved by microscopic section. Bick has emphasized the occurrence of pain in an ulcer or sinus after a period of quiescence as suggestive of the onset of malignancy.

The prognosis on the whole is relatively good, because of the long slow course of the disease before extension and metastasis occur. However, the carcinoma is invasive and produces lymph node and organic metastases if not removed, and the prognosis depends upon the stage at which the lesion comes under adequate treatment, on the presence of lymph node involvement, infection, multiplicity of lesions, etc. In a study of 134 cases (exclusive of roentgen carcinoma) of all stages a favorable outcome was found to be reported in 65 per cent. When we begin to break down the statistics according to etiologic factors, we find that the best prognosis is offered by those cases in which the carcinoma arose on previously normal skin without any known preceding factor. The next best prognosis is in those cases in which the carcinoma followed some of the various irritative lesions noted above. Carcinoma arising from a previously present neoplasm or wart presents the worst prognosis and if the original neoplasm has been congenital the outlook is as bad as for the malignant melanomas.

Despite the rarity of metastases, the prognosis for lupus carcinoma is not favorable. Of Mündelein's 83 cases, 39 died of their carcinoma, 4 were inoperable, and 8 refused treatment. Of the remaining 42 patients, 14 only were free of recurrence at the time of his report and of those only 3 had been under observation for five years or over.

The presence of lymph node involvement, whether this be proved to be due to carcinoma or not, definitely impairs the prognosis. While the presence of enlarged lymph nodes does not prove that metastases are present, the absence of lymph node enlargement is rather good evidence that there is no metastasis. In no recorded instances in which the glands were not palpable before operation and were dissected out were they found to be invaded. DeBell and Stevenson have made the same observation. When glandular enlargement is present, there is failure to obtain successful result in nearly 60 per cent, while if glands are not present this figure is reduced to 25 per cent.

The treatment of the isolated lesion will depend upon its extent. It is my feeling that surgical removal is to be preferred to diathermy or cautery destruction, and in this I agree with DeBell and Stevenson. The small lesions on the dorsum of the hand usually can be excised and the resultant defect sutured. It is seldom possible, however, to excise lesions on a finger and close the defect by suturing since the skin here cannot be sufficiently relaxed and often even small excisions must be closed with a graft. Large carcinomas which have remained

## SUBUNGUAL MELANOMA\*

### THE DIFFERENTIAL DIAGNOSIS OF TUMORS OF THE NAIL BED

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IN 1886 Jonathan Hutchinson described melanomas of the nail bed, to which he applied the term melanotic whitlow. In explanation of this nomenclature, Hutchinson said: "Because it resembles whitlow and is usually so named at first, I prefer to give it that name." The same lesion has been designated by various synonyms, such as onychial melanoma, subungual melanoma, and melanocarcinoma, melanosarcoma, or melanoblastoma of the nail bed. This regional occurrence of melanomas provides an interesting clinical study.

Subungual melanoma is rare in comparison with other diseases of the nail. Pardo-Costello found only 1 subungual melanoma among 94 patients with nail diseases seen during a period of six months. White found no melanomas among 485 patients with nail diseases treated during three years at the Massachusetts General Hospital and in private practice.

A small proportion of melanomas are subungual in location. In 1932 Farrell reported on 265 cases of melanoma, 6 of which were subungual; and Affleck, in 1936, found the same number in a total of 266 cases. In a report published from the Memorial Hospital in 1930, there were 4 subungual melanomas in 218 melanomas of all locations. Continuing this report through the year 1937, to cover the twenty-one years since 1917, our figures show 477 cases of melanoma. The 16 subungual melanomas represent 3.4 per cent of the total.

The average age of our patients with melanomas of various regions was 47.9 years. For the patients with subungual melanoma it was somewhat higher, namely 58.7 years. This is consistent with the data available for 48 of the cases reported in the literature, their average age being 55.9 years. For our group the range was from 30 to 71 years; for the reported cases, from 23 to 80 years.

The sex was given for only 55 of the reported cases, 26 males and 29 females. In our series there were 10 males and 6 females. Of the total cases, therefore, slightly more than one-half were males.

The frequency with which the various digits are the site of subungual melanoma is shown in Table I.

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layer of which is continuous with the matrix. The nail bed plays no role in the formation of the nail plate, but it is a corium rich in nerves and blood vessels, which are important in maintaining the nutrition of the nail.

Hutchinson's description of the appearance and behavior of these so-called melanotic whitlows is well worth quoting: "It needs sometimes the eye of faith to recognize the narrow band of black which borders the inflamed part. It would seem that the power to produce a pigmented structure is but feeble in the neighborhood of the nails; whenever there is much growth, a nonpigmented mass is produced. The mixture of colored and uncolored growth in melanotic sarcoma is of course common in all parts, but in none is it, I think, so marked



Fig. 1.—Subungual melanoma. Note the pathognomonic border or halo of black pigment at the edge of the involved nail.

as in the proximity of the nails. The disease is slower in its stages than is the case with melanosis in most other positions. So far as I know, the growth presents no histologic peculiarities. Yet there is much greater hope of delaying the progress of the disease by operation than exists in most other forms of melanosis."

The fully developed lesion is usually a black, fungating, well-demarcated ulcer, involving the nail sulcus and matrix and elevating the nail. The nail itself becomes thickened, brittle, split, and finally ulcerated. The melanoma sometimes has the appearance of purplish granulation tissue, flecked with small areas of scattered black pigment. A pathognomonic point in diagnosis is a border of coal black color which is nearly always present at the edge of the involved nail (Fig. 1). An important point concerning the early gross appearance is the fact that the tumor seems to be independent of the skin, grow-

TABLE I

SITE	TOTAL CASES	REPORTED CASES	MEMORIAL HOSPITAL CASES
Total	85	69	16
Hand (total)	48	38	10
Thumb	27	22	5
Finger	19	14	5
Not specified	2	2	
Foot (total)	37	31	6
Great toe	34	30	4
Toe	3	1	2

Of the subungual melanomas reported in the literature, the great toe was the most frequent site, with 30 cases, followed by twenty-two located on the thumb. In our experience they are more frequent on the hand.

Melanoma in general is more common on the foot than on the hand. Of our 477 cases of melanomas of all locations, 74, or 15.5 per cent, were located on the foot, with the 6 subungual melanomas, 8.1 per cent, of the 74. Only 29 of the 477 tumors, or 6.1 per cent, occurred on the hand, with 34.5 per cent of these subungual in location.

Melanomas are comparatively rare in the negro, with the exception of certain reports from Africa. Thirty-four have been reported in the literature, excluding the African natives. Melanomas in negroes tend to develop in those parts of the body which contain the least pigment; e.g., on the soles of the feet. The matrix of the nails in negroes is not so deeply pigmented as the skin, which is significant in view of the relative frequency of subungual occurrence. There were 7 negroes in our series of 477 cases, only 1 of whom had a subungual melanoma, located on the thumb. Bauer reported 2 cases of subungual melanoma in negroes, 1 on the thumb and 1 on the great toe; Dickson and Jarman, 1 on the finger; and Hewer, reporting on 47 melanomas seen in Khartoum in the five years from 1929 to 1934, found 2 cases occurring in the nails of the fingers.

A consideration of the anatomy of the nails is of interest before discussion of the clinical appearance of subungual melanoma. The nail and nail bed are epidermal and dermal appendages very much like the hair follicle in genesis. The nail is the analogue of hair; and the nail matrix, of the germinative layer of the hair follicle. The follicle in primitive animals is a tactile end organ with abundant nerve supply; the nail bed also is exquisitely sensitive and contains numerous tactile end organs. Some of these are involved in the genesis of melanoma, which is essentially a tumor of the end-organ apparatus. As will be mentioned later, the glomus is another peculiar structure found in the nail bed which may undergo neoplastic changes. The nail matrix is the only reproductive portion of the nail and it bears a close morphologic resemblance to the stratum malpighii of the skin. The hyperkeratotic nail plate overlies the nail bed, the epithelial

features of these infections which serve to differentiate them from melanoma. If melanotic whitlow is unrecognized and the treatment is the same as for paronychia, a fungating lesion soon develops, with loss of the nail and invasion of the regional lymph nodes. Chronic osteomyelitis secondary to or independent of felon may so disturb the appearance of the nail and nail bed as to simulate a neoplasm (Fig. 2). Lateral roentgenograms of the terminal phalanx should be made in the case of all subungual tumors.

2. *Pyogenic Granuloma*.—The simple papillary granuloma is of frequent occurrence about the nail sulci (Fig. 3). It is soft and extremely



Fig. 2.—Osteomyelitis of terminal phalanx simulating subungual melanoma.

vascular. There is an abrupt, sharp, punched-out line of demarcation between the tumor and the skin which surrounds it. It grows rapidly, recurs usually after attempted surgical removal, and disappears, as if by magic, following the application of a small dose of roentgen-ray or radium therapy. Its radiosensitivity, evolution, and appearance are points of diagnostic importance.

CASE REPORT.—E. S., a 9½-year-old girl. A small subungual wart on the end of her finger became infected when she squeezed it. It increased in size and involved the distal phalanx of her finger (Fig. 3). A roentgenogram at another hospital was negative for osteomyelitis.

Low voltage x-ray therapy, 1,500 r. units, in one dose was given to the finger with good results.



ing from beneath, displacing, and elevating the eponychium. In the early stages the surface epithelium is intact. About the time of ulceration, pigmented streaks often appear in the skin surrounding the tumor. From the ulcerated surface a thin dark fluid exudes which stains the dressings and becomes brown, like melanotic urine on exposure to air. The local lesion is limited in the direct extension of its growth by the fascial planes of the distal phalanx in a manner similar to that seen in infections. The melanoma begins in the nail sulcus more frequently than in the middle of the nail bed.

The predominant cells of these subungual melanomas are of two types: (a) the fusiform spindle cells, with hyperchromatic nuclei, intra- and extracellular pigment, and infrequent mitoses (the melanoma of this histologic variety is frequently called melanosarcoma); (b) the spherical, polygonal, or epithelioid cells, often in sheets and pseudoalveolar arrangement, with less pigment and more frequent mitoses (the melanoma of this histologic variety is often termed melanocarcinoma). Regardless of the histologic picture and cell type, all the subungual melanomas pursue the same clinical course and metastasize by way of the lymphatic vessels to the regional lymph nodes. The melanoma cell emboli usually skip the cubital and popliteal lymph nodes to lodge in the axillary and inguinal lymph nodes. The metastatic tumors frequently are darker than the primary melanomas of the nail bed.

A pigmented spot under the nail may remain quiescent for a long time, as is characteristic of pigmented naevi in other parts of the body. In Boyer's patient it was inactive for twenty-eight years. The onset of true melanoma may be a slow insidious development, but once the tumor begins to grow and assert its malignant properties, the ensuing course may be fairly rapid. Pain is never conspicuous, even as a late symptom.

#### DIFFERENTIAL DIAGNOSIS

The most important problem concerning subungual melanomas is the correct early diagnosis. Failure to diagnose correctly frequently may mean that the favorable time for operation has passed. Many patients are at first treated for infection. An examination of the blood is of no help, and black coloration of the urine is a late phenomenon. In general, the subungual melanomas may be differentiated from benign tumors in that the latter do not break through the nail. It is essential to distinguish this tumor from the following pathologic lesions of the same location:

1. *Paronychia; Whitlow or Felon; Osteomyelitis.*—The age of the patient, antecedent history, absence of pigmentation, acute onset, acute tenderness, pain, redness, purulent discharge, and rapid course are

whereas onychomycosis generally is distributed about other nails of the same hand or foot. The two diseases may be coexistent, since ringworm of the nails is such a common infection (Fig. 4, Case 10).

4. *Subungual Hematoma*.—A black or brown melanotic spot under the transparent nail may resemble the black ecchymotic area of old extravasated blood following an injury. The importance of the differential diagnosis in this instance lies in the fact that hematomas of the nail bed are common and trauma seems to be an occasional inciting factor in subungual melanomas. The definite history of antecedent trauma, the color changes characteristic of a bruise, and the suffusion of blood into the surrounding integument identify the lesion as a hematoma. Under the mistaken diagnosis of subungual hematoma, surgeons have drilled holes through the nail plate in order to evacuate supposed blood clot, only to have the unsuspected melanoma fungate out through the nail.

5. *Primary Syphilitic Chancre of Finger*.—The history of exposure (usually in a physician), the location in the nail sulcus, the rapidity of growth, the absence of pigmentation, and the recognition of the *Spirochaeta pallida* on dark-field examination are significant differential points of diagnosis.

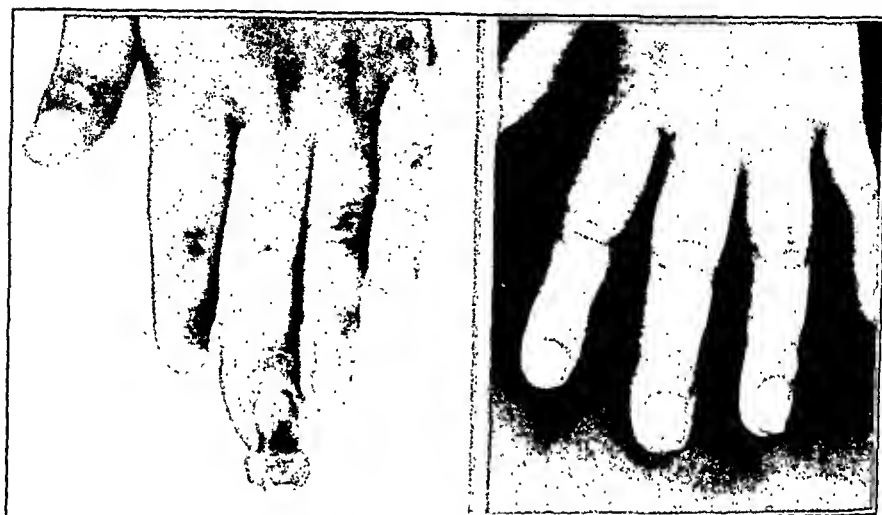
6. *Gangrene of the Toe*.—A careful general physical examination always furnishes confirmation of the diagnosis of gangrene of the toes. The patients are usually older than the subjects with subungual melanoma. Coexistent with the gangrene are often such related findings as diabetes mellitus, arteriosclerosis, and hyperpiesia. Gangrene is frequently bilateral and may involve more than one toe. The prodromes of numbness, tingling, and paresthesia and the local picture of the gangrenous lesion are additional diagnostic points in the recognition of gangrene.

7. *Dupuytren's Exostoses* (subungual osteochondromas) of the terminal phalanges are easily recognized on radiographic examination. The greatest difficulty in diagnosis arises in the early tumors in which ossification has not occurred. Lateral roentgenograms reveal the tumor which otherwise may be hidden. It cannot be palpated because of protection by the overlying nail. The true nature of the tumor may be obscured by the common coexistence of marked subungual hyperkeratosis, which seems sufficient on casual inspection to account for the distortion of the nail. (Fig. 5.)

8. *Subungual Fibroma*.—This benign nonpigmented inactive lesion is readily recognized but occasionally required a biopsy for confirmation of the diagnosis. It may be a neurofibroma in some cases; in other instances it is a foreign body reaction about an imprisoned thorn or splinter.

9. *Subungual Keratosis*.—Due to trauma, irritation by a foreign body, or recurrent ringworm infection, the nail may become elevated

3. *Onychomycosis Nigrescens*.—A parasitic fungus of the ringworm family which occasionally involves the nail and matrix. Because of the production of black pigment, it is easily mistaken for subungual melanoma.



A.

B.

FIG. 3.—A, Pyogenic granuloma before radiation therapy; B, pyogenic granuloma after radiation therapy.

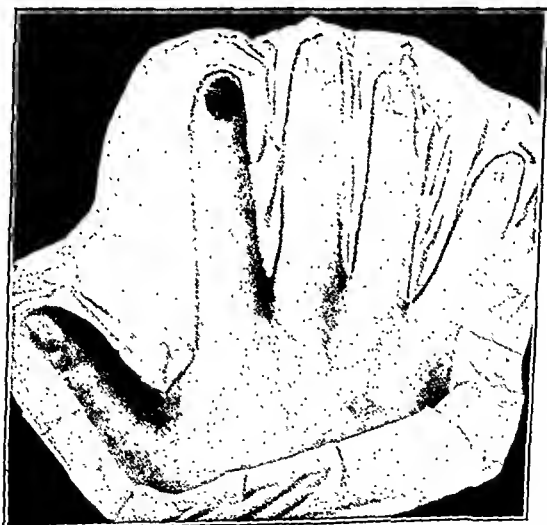


FIG. 4.—Case 10. Moulage of hand showing subungual melanoma. A black pigment-producing fungus was isolated from scrapings of this nail.

noma. Microscopic examination of the nail scrapings dissolved in potassium hydroxide solution reveals the presence of the fungus in a certain number of cases. Subungual melanoma involves only one nail bed,

of the toe was a sessile, elevated nodule, measuring 1 cm. in diameter (Fig. 6). It was bluish in color and had some of the clinical features of subungual melanoma. A biopsy was taken; the diagnosis was keratosis. Treatment consisted of a square radon plaque applied for 800 mc. hours at 1 cm. distance, and a radon bulb applied for 500 mc. minutes. Later the nail bed of the great toe was excised. There has been no recurrence.

10. *Subungual Epithelioma*.—With this tumor the nail sulcus rather than the matrix is involved. The epithelioma grows more slowly, ulcerates more quickly, and bleeds less easily than the melanoma of the same location. It differs from the melanoma in being firmer, non-pigmented, and frequently papillary in structure. The epithelioma may be one of many epitheliomas of the skin in the same subject and is frequently associated with such diseases as Bowen's preancerous keratodermas and Darier's carcinoma cutis multififormis verrucosis. Biopsy may be necessary at times in order to plan the method of treatment, as epithelioma usually responds well to radium therapy, whereas melanomas are notoriously radioresistant. We have seen this cancer develop beneath the nails of radiologists afflicted with chronic radiation dermatitis.

11. *Subungual Angiosarcoma (Kaposi's disease)*.—This rare tumor is of comparatively slow growth, red and vascular, nonpigmented, and soft. The tumor cells are arranged about the blood vessels in such a manner as to suggest a peritheliomatous origin. Although melanoma metastatic to lymph nodes may resemble primary angiosarcoma of the lymph nodes in histologic appearance, the primary melanomas and angiosarcomas of the nail bed are more obviously distinct clinical and pathologic entities. Kaposi's sarcoma occurs usually on the lower extremities of males, generally those of Slavic, Jewish, or Southern European origin. The tumors are multicentric in origin, so that more than one primary site may exist. They may occur bilaterally. These patients usually have short, thick legs with associated varicosities and occasionally edema of ankles and feet. Other regions on the hands and feet, in addition to the nail bed, are involved. The first lesion is a macule, which under the microscope appears to consist of ectasia of blood vessels and perivascular lymphocytic infiltration. The second stage is an elevated nodular granuloma which does not seem neoplastic. Finally the nodules become confluent and firmer; under the microscope the tumor has protean characteristics, varying in the quantity of angiomatous, myomatous, and neuromatous elements, so that it may resemble a peculiar angioma, or angiosarcoma, endothelioma, fibroma, fibrosarcoma, leiomyoma, etc. The tumor originates probably from the region of the complex neurovascular annexes. Treatment is usually by radiation therapy.

CASE REPORT.—Dr. J. M., aged 54 years. Ten weeks previous to diagnosis he noticed a small ulcer near the lateral sulcus of the nail bed of the middle toe of the right foot. This gradually increased in size and recently had bled. It had not been

and distorted by hyperkeratosis occurring beneath the nail or in the sulcus. Occasionally it is pigmented. It may be precancerous.

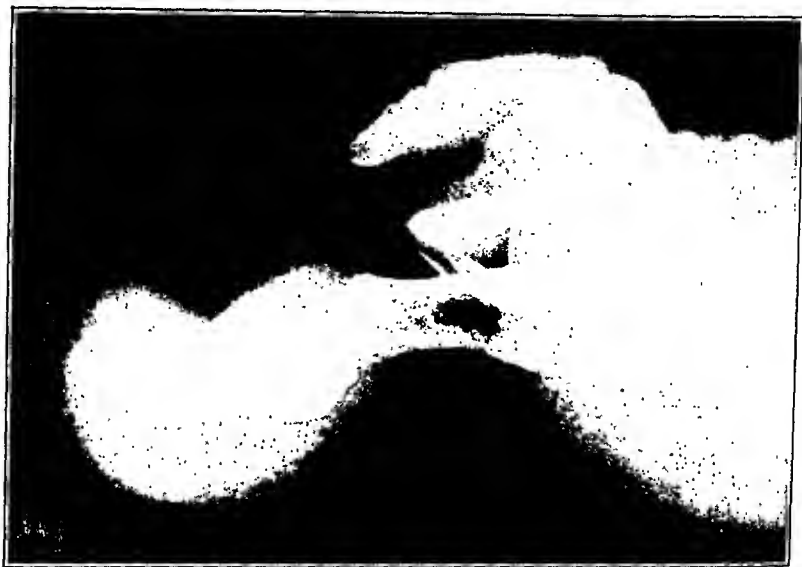


Fig. 5.—Dupuytren's cartilaginous exostosis of terminal phalanx (subungual).



Fig. 6.—Subungual keratosis simulating melanoma.

CASE REPORT.—Mrs. B. B., aged 40 years. In October, 1935, the patient discovered a small black spot under the medial side of the right great toenail. There were occasional pain and some discharge simulating infection. Arising from the matrix

exquisite sensitivity of glomus tumors are important diagnostic criteria. They give rise to sharp, radiating pain, spontaneous in occurrence.

CASE REPORT.—D. H., a physician, aged 48 years. In the posterior portion of the nail of the index finger of the left hand was a rounded tumor lying beneath the nail and measuring about 6 mm. in diameter. It was elevated but slightly, causing a change in the nail bed and the nail from that point forward to the tip of the nail. It was extremely tender to touch. It was deep rose in color. It was a typical glomus tumor, small when first noticed. The patient had scraped and split the nail, relieving the pressure.

Radiation therapy was given first at the patient's request. Five months later the nail was split and in bad condition due to radiation. The patient did not come to a decision as to whether or not the nail was to be removed.

13. *Metastatic Tumors of the Nail Bed.*—This occurrence is so rare as to constitute a curiosity. There have been only 2 such instances in our experience.

CASE REPORT.—M. G., a woman aged 41 years, gave the following history: In 1928, shortly after confinement, she noticed a small lump back of her right ear. This gave no trouble until 1933 when it began to grow. On March 17, 1934, she consulted her physician when the tumor was 4 cm. in diameter. The mass was removed by him on April 2 and proved to be closely adherent to both skin and fascia. The facial nerve was involved and so was sacrificed. The diagnosis was adenocarcinoma of the parotid. On April 13 she was referred for postoperative radiation treatment: radium element pack 24,000 mg. hours at 6 cm. distance, followed by the insertion of gold radon seeds on Oct. 16. On Sept. 20, 1935, there was no evidence of recurrence.

In August, 1935, she crushed the middle finger of her right hand, but noticed nothing unusual at the time other than local pain and discomfort. About Dec. 20 she observed that the finger was becoming tender, swollen, and reddened, with infection in the nail bed. She applied for treatment Feb. 20, 1936.

The infection involved the lateral sulcus and discharged considerable pus. Roentgenograms were made, with a provisional diagnosis of osteomyelitis of the terminal phalanx. On the suspicion that it might be due to metastasis, the lateral third of the nail bed was excised down to the nail sulcus, and immediate frozen section confirmed the diagnosis of carcinoma. An amputation of the distal phalanx was performed, using a ventral flap. On April 3, 1936, the finger was almost healed and there was no evidence of a recurrence of the parotid tumor.

On June 5, 1936, there was a subcutaneous nodule 1 cm. in diameter situated in the side of the finger which was amputated. There was a very large freely movable lymph node in the right axilla.

On June 6, 1937, a left thoracentesis was performed. Death occurred on Oct. 20, 1937. The diagnosis was adenocarcinoma of the right parotid gland with generalized metastases.

#### THE PROGNOSIS OF SUBUNGUAL MELANOMA

The prognosis of patients with subungual melanomas depends on the presence or absence of metastases to the regional lymph nodes. Melanomas of the nail bed are seen early by the patient because of their conspicuous location, but they are diagnosed by the physician at a late stage in their course because of their confusing resemblance to other

painful. There was no history of injury (Fig. 7). A biopsy was taken; the diagnosis was Kaposi's sarcoma. Square radium plaque for 800 mc. hours at 1 cm. distance was given on Nov. 14, 1935.

On April 9, 1937, there was a nodule measuring  $\frac{1}{2}$  cm. in diameter on the medial aspect of the left great toe, which was elevated and fiery red. This was excised on April 9. On April 14 a square radium plaque was applied to the toe for a dose of 750 mc. hours. No new nodules have occurred to date.

12. *Subungual Tumors of the Glomus.*—In 1924 Masson described 3 cases of small bluish tumors, subungual in location and exquisitely sensitive. Masson has shown that these tumors arise in organs situated in the field of certain arteriovenous anastomoses and demonstrated nerve

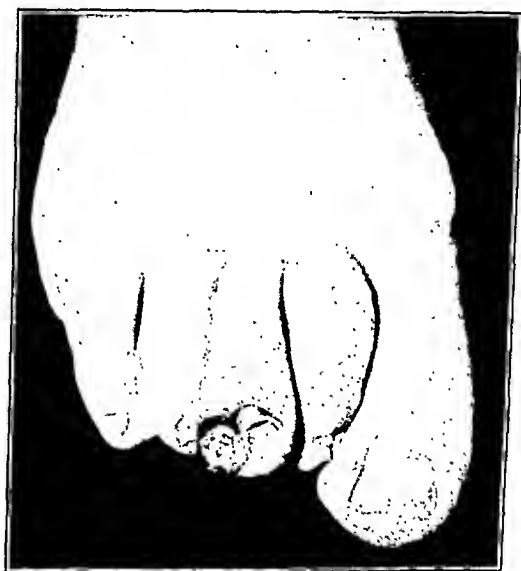


Fig. 7.—Kaposi's hemorrhagic sarcoma developing in nail sulcus.

fibers surrounding the vessels of the tumor, applying to the organ the term "glomus neuromyoarterial." Histologically, the epitheloid cells of Masson surround the arterioles of the glomus, where they intermingle with smooth muscle cells. This vascular neuromuscular organization (glomus) is normally pulsating and aids in regulating the blood pressure to the extremities. The glomus tumors develop most frequently in the nail bed and about the fingers and toes, where the glomus occurs with greatest frequency. In 1936 Geschickter analyzed the 78 verified cases in the literature of tumors of the glomus and found that 22 of the 31 on the fingers were subungual. This is the only tumor in this group which may cause some difficulty in the diagnosis of subungual melanoma. A positive diagnosis can be made only with the microscope. The benign nature, slow growth, absence of metastasis, and

reaction occurs, it is often followed by late radioneerosis and a painful useless finger tip or toe. Preoperative irradiation is no longer employed for melanomas of this particular location.

*Necessity for Early Amputation.*—Once the diagnosis of subungual melanoma is made, amputation of the digit should be considered as an emergency, because the day or time of the metastases can never be foretold. The number of phalangeal joints to be sacrificed depends on the proximal extent of the tumor. Conservative surgical excision with preservation of the terminal phalanx is hazardous.



FIG. 8.—Recurrent myxomatous cyst of nail bed and nail matrix.

*Prophylactic Dissection of Regional Nodes.*—A study made two years ago of all malignant melanomas of the extremities revealed the distressing information that radical dissection of the primary melanoma often was not curative in itself, even in patients in whom no regional lymph nodes were palpable. Some of these patients would return during their observational period with large confluent nodes containing metastatic melanoma which was not observed at the previous visit. The decision was made to dissect out the regional lymph nodes as a routine procedure even if the nodes were not palpable. The wisdom of this routine practice has been proved by the subsequent micro-



lesions in the region of the nails. Fourteen of the sixteen patients studied at the Memorial Hospital had enucleations of the nail beds in other clinics prior to the determination of the correct diagnosis. Incision and enucleation of these so-called black cancers are hazardous procedures because they facilitate infection of the tumor and probably hasten the dissemination of the melanoma by metastasis to other regions.

The percentage of cures for subungual melanomas is higher than for melanomas of any other location. The reason for this advantage is not only the slow rate of growth and the late period of dissemination of these tumors, but also the unique location at the terminal ends of the phalanges. This situation is such that amputation of the involved region is usually a curative procedure if no metastases have occurred. Melanomas of other locations are not so amenable to radical surgical extirpation unless crippling deformities or extensive loss of tissue are suffered. The end results are summarized in Table II.

TABLE II

END RESULTS OF SUBUNGUAL MELANOMAS TREATED AT THE MEMORIAL HOSPITAL, 1917 TO 1937, INCLUSIVE

PREVIOUS TREATMENT AND CONDITION AT TIME OF ADMISSION TO MEMORIAL HOSPITAL	TOTAL	DEAD	ALIVE*	
		WITH RECURRENCE	WITH NO EVIDENCE OF RECURRENCE	WITH RECURRENCE
Total	16	8	5	3
1. Amputation elsewhere, with involvement of nodes on admission	7	6 mo. (5 cases)	15½ yr.	2¾ yr.
2. Curettement elsewhere with involvement of nodes on admission	3	4 mo. 1 yr.	8 yr and 7 mo.	
3. Curettement elsewhere, with no involvement of nodes on admission	4		5 mo. (under treatment) 2½ yr. 9¾ yr.	5¼ yr.
4. No previous treatment, except salves, with no involvement of nodes on admission	2	3¾ yr. (immediate recurrence)	2 yr.	

\*Five-year survival: Alive, with recurrence, 1 (6.25 per cent); alive, with no evidence, 3 (18.75 per cent)=4 (25 per cent).

## TREATMENT

All reported cases of subungual melanoma have been treated by surgical intervention. Malignant melanomas of all locations are notoriously radioresistant and those located in the nail bed are doubly so because of their situation. The nail bed is not a good tissue for the reaction which accompanies curative doses of radiation. The dose of radium or roentgen rays necessary to sterilize a subungual melanoma must be almost caustic in effect. If primary healing of the radiation

method of surgical treatment, they may grow in blocked lymph vessels or be emptied into a fresh wound.

The following case reports represent the different groups included in Table II:

*1. Amputation Elsewhere With Involvement of Regional Nodes at the Time of Admission to the Memorial Hospital.—*

CASE 1.—M. V. T., a woman 40 years of age, applied to the Memorial Hospital Nov. 7, 1933.

Four years before the patient had had a slight injury to her left index finger-nail. She thought a splinter was lodged therein. There followed a long series of treatments for paronychia infection. About twelve curettements of the nail bed were done for more than three years. The terminal phalanx finally was amputated. Six months later the terminal portion of the amputated finger became enlarged, red, and extremely painful. Following this a second amputation was done so that the second phalanx was removed. Within a few more months the proximal phalanx was removed.

During the last year the patient noted the continuous appearance of new subcutaneous nodules in the palm, forearm and arm, left chest wall, left abdominal wall, scalp, and left back. Some of these nodules have been excised and others treated by the insertion of gold seeds. The regression of the nodules treated by radiation indicated that the tumor had at one time been rather radiosensitive.

In the scalp there were from six to eight subcutaneous nodules varying from 4 to 8 mm. in size. In the left palm and in the subcutaneous tissues of the left forearm and arm there were about twenty subcutaneous nodules, the largest of which was 2 cm. in diameter. The abdomen showed no enlargement of the liver or palpable masses. A diagnosis was made of malignant melanoma with dissemination.

Palliative doses of roentgen rays and radium were given to all the known melanotic nodules during the next three months. There was no appreciable local or constitutional benefit.

Her condition was unimproved. The patient died on Nov. 7, 1933.

CASE 2.—R. B., a male aged 53 years, applied to the Memorial Hospital Sept. 14, 1931.

In 1925 a sore appeared under the nail of the great toe of the right foot. The nail crumbled. Iodine was applied, which desiccated the sore. The nail grew out again and a discharge appeared. The nail was removed and the nail bed scraped. When the nail grew out again, the discharge recurred. From 1926 to 1928 there were several curettements. In 1930 x-ray treatments were given, with no response. In January, 1931, there was evidence of metastasis to the right groin. In April, 1931, the matrix of the diseased nail was cut away. In June, 1931, there was swelling of the left cervical lymph nodes. In August, 1931, a roentgenogram of the chest revealed pleural metastasis. The patient coughed up black clotted blood.

On admission the right toe had been amputated through the distal joint, with no recurrence in the stump. Dotted over the patient's trunk, arms, and thighs were numerous subcutaneous, firm nodules, spherical and oval, varying from 0.5 to 3 cm. in diameter. Some of the smaller nodules were surrounded by zones of ecchymosis. In the right groin was a group of enlarged elastic nodes and in the left supraclavicular space was a mass 5 cm. in diameter over which the skin was reddened.

scopic studies of these lymph nodes removed prophylactically; in two-thirds of the cases minute foci of metastatic melanoma (clinically undetectable) were found (Case 14). Therefore, the dissection of lymph nodes is performed in all patients, whether the lymph nodes are enlarged or not.

*Interval Between Amputation and Regional Lymph Node Dissection.*—Another observation has been that an element of danger exists in performing both the excision of the primary melanoma and the dissection of regional lymph nodes at the same operative séance. This procedure

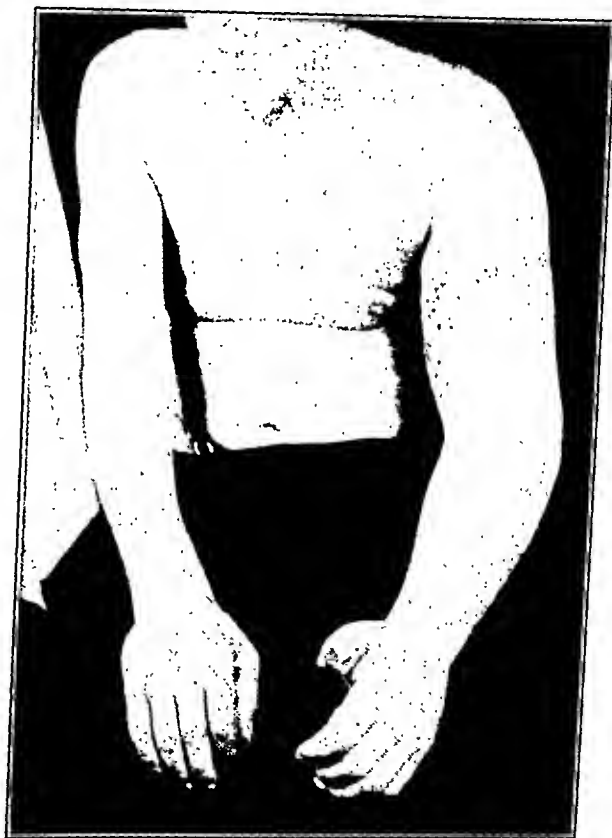


Fig. 9.—Recurrent melanoma of arm, thumb, and axilla.

has been followed too frequently by the development of new melanotic nodules in the intervening limb or by diffuse recurrence in the axillary or inguinal wounds (Fig. 9). The practice now is to amputate first, then perform the regional lymph node dissection one to two weeks later if there is gross evidence of metastatic involvement and six weeks later if the dissection is considered prophylactic. If melanoma cells are in transit in the lymphatics, they may be filtered out in the lymph nodes during this time; whereas, in the previously stated

The patient's general health had been excellent until about two weeks prior to admission to the Memorial Hospital, when she noticed shooting pains under the right armpit, and about ten days later there was a hemorrhagic discoloration of the skin of the right breast. She noticed the coincidental presence of a mass in the right axilla. She was referred from another hospital for further treatment.

Examination showed no evidence of recurrence in the right index finger. In the right axilla was a bulky indurated movable mass measuring about 6 by 8 cm. in diameter. The skin of the tail of the right breast was yellow and erythematous in blotchy areas. A film of the chest showed a small circular shadow of increased density measuring about 1 cm. in diameter in the lateral portion of the right subapical region, with another nodule, somewhat larger in size, just lateral to the lower pole of the left hilus region. These nodules represent metastases.

On March 14, 1934, a palliative left radical mastectomy was performed. Convalescence was uneventful.

On May 5, 1934, the patient was admitted to the observation ward at the Bellevue Hospital. From there she was transferred to the Manhattan State Hospital where she died on June 15, 1934. The diagnosis was psychosis with cerebral arteriosclerosis.

CASE 5.—G. S., a machinist, aged 62 years, applied to the Memorial Hospital on Oct. 10, 1934.

In March, 1933, the patient hit his thumb with a hammer. The blow knocked off part of the side of the thumb, leaving a raw bleeding area at one side of the nail. The lesion never healed, but slowly increased in size, forming a cauliflower tumor which bled easily and was dark in color. In August, 1933, the thumb was amputated. At this time a tumor developed in the left forearm and a tumor in the left axilla was noted. A month later axillary dissection was done. The patient was free of symptoms for several months. Then the tumor recurred under his arm, growing steadily, and the tumor on the forearm increased in size.

Examination revealed the left thumb missing beyond the interphalangeal joint. On the skin of the forearm about midway between the wrist and the elbow over the radius was a tumor 2 cm. in diameter. The tumor in the left axilla measured 18 by 13 by 22 cm.

X-ray treatment in fractionated doses was given from Oct. 11 to Oct. 25, 1934, to the left shoulder girdle, anterior, posterior, and lateral fields.

The general condition of the patient was not good enough to permit an interscapulothoracic amputation.

On Jan. 7, 1935, the patient complained of pain in the small of the back, suggesting involvement of the lumbar vertebrae. There was a bulky axillary and left supraclavicular involvement and many skin nodules on the left chest wall as well as the upper arm. The liver was greatly enlarged, and the patient was considered to be in the terminal stage. He died on Jan. 26, 1935.

CASE 6.—F. W., a physician, aged 71 years, applied to the Memorial Hospital, March 18, 1935.

In 1887 an ingrown nail on the right big toe was removed but the matrix continued to grow. This overgrowth of the matrix was removed in 1933. The nail did not grow and an ulceration appeared over the nail bed. This bled easily and an offensive discharge was constantly present. During the course of a year, he received two x-ray treatments and one radium pack treatment. The lesion healed temporarily. In 1934 the first toe was removed with resection of the inguinal lymph nodes. The patient then went to England where he had resection of the femoral lymph nodes and x-ray therapy over the iliac region, two ports, anterior and

Certain facts in this case, such as the widespread rapid dissemination, the occurrence of ecchymosis accompanying the appearance of new nodules, the fact that the patient had noticed spontaneous regression of some nodules and that he noted some regression of the tumor in the right groin following x-ray treatment, all suggested that this melanoma might be somewhat more radiosensitive than usual.

He was admitted to the ward for continuous irradiation to the entire body by the Heublein unit, Sept. 15 to Oct. 12, 1931, 523 hours, 225 r. On Nov. 3 new metastatic melanomas appeared, and the patient gradually became worse. At his own request, on Nov. 14, the patient was transferred to a hospital in Connecticut where he died on Dec. 9.

The autopsy report showed the following organs involved: sternum; pleural surface of the pericardium over the right auricular region; heart, just under the endocardium, in the right auricle a small tumor; lungs; abdomen, chiefly in the mesentery of both large and small intestines; extensive involvement of the retroperitoneal lymph nodes, the urinary bladder, and kidney.

CASE 3.—E. W., a negro male laborer, aged 59 years, applied to the Memorial Hospital on Aug. 2, 1928. He had always been in good health until the present illness.

Early in 1926 he injured his left thumbnail. After some palliative treatment, the nail was removed, but the lesion grew rapidly to involve the entire distal phalanx. At another hospital in December, 1927, an amputation was performed at the metacarpophalangeal joint. The wound healed satisfactorily by primary intention. In May, 1928, the patient felt a small mass in the left axilla, which grew rapidly.

On examination at the Memorial Hospital, the wound at the base of the left thumb appeared to be healed with no evidence of disease. In the left axilla there was a hard, fixed, inoperable mass composed of fused nodules the size of an orange. The mass extended anteriorly and subpectorally. There was free arm motion. Another node was felt in the supraclavicular region. A radiograph of the chest was negative for metastasis.

Microscopic examination of the tumor of the thumb showed a melanoma composed of interlacing fusiform cells with hyperchromatic nuclei and abundant intra- and extracellular pigment. There were frequent mitoses. The cells were arranged in infiltrating strands and whorls, characteristic of melanosarcoma. The diagnosis of melanoma was confirmed by Dr. Ewing.

The left axilla and left supraclavicular space were treated by combined external irradiation, using high voltage x-rays and the radium element pack.

On Oct. 24, 1928, the axillary and supraclavicular nodes appeared slightly smaller. On Nov. 28, 1928, the axillary tumor showed definite diminution in size, but both supraclavicular fossae contained hard palpable nodes. On Jan. 1, 1929, information was received of the patient's death. In the terminal period of his disease he suffered severe pain in his head, particularly at the base of his skull. No necropsy was performed.

CASE 4.—C. D., an Irish woman, 46 years old, applied to the Memorial Hospital on March 13, 1934.

A window sash had fallen on her finger about a year previously, and for about a month afterward the finger was black and blue, quite painful, and swollen. This disappeared, but a few weeks later there was a blackish blue discoloration of the nail bed extending into the skin around the base of the nail. There was occasional bleeding but never any formation of a demonstrable tumor or an ulcerated lesion. In October, 1933, amputation was performed, at the interphalangeal joint, followed by an uneventful convalescence.

The examination revealed the nail absent from the left thumb, an atrophic appearance of the entire thumb, the skin smooth and epilated. The nail bed had a granular appearance and in the center of it was a rounded firm granular tumor

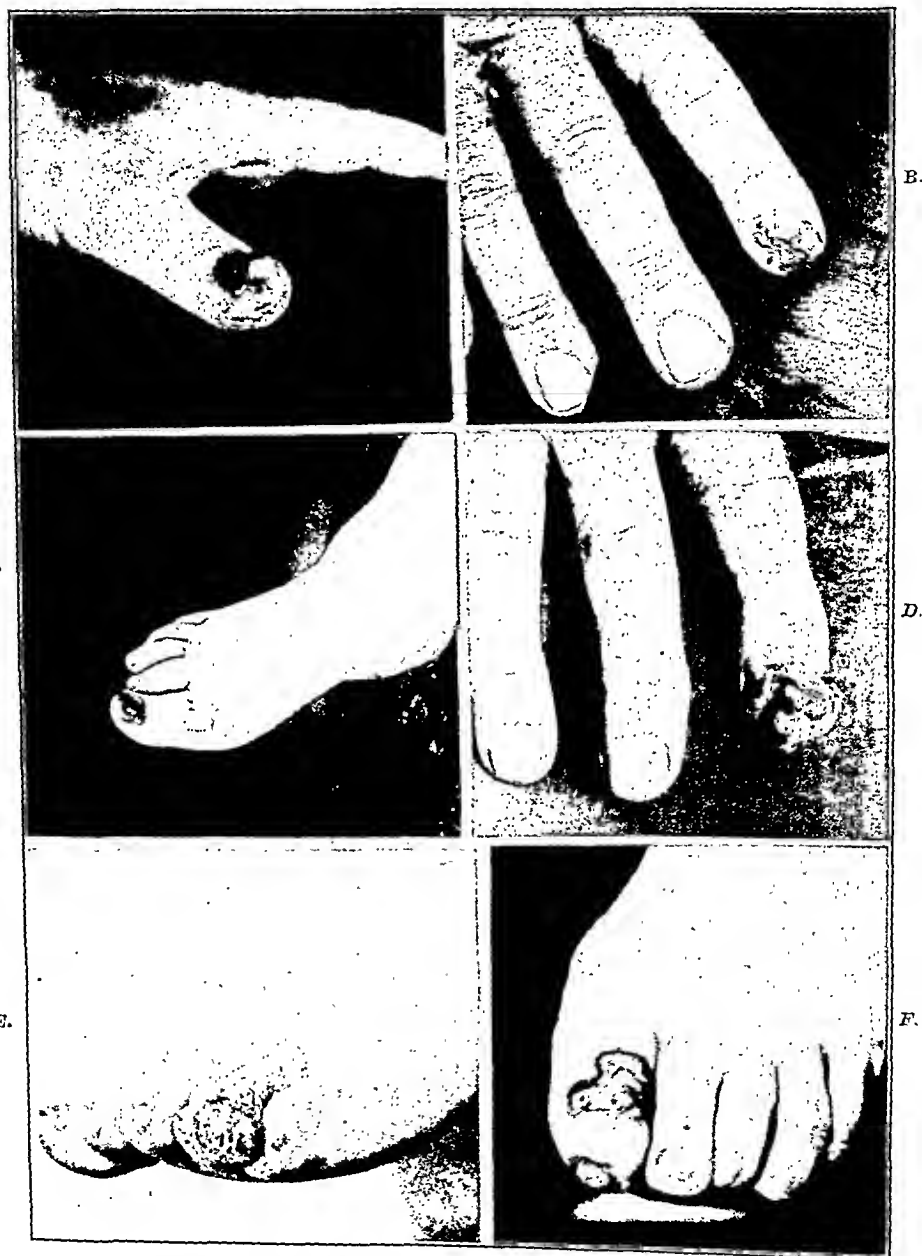


Fig. 10.—Subungual melanomas. A, Case 8; B, Case 11; C, Case 13; D, Case 14; E, Case 15; F, Case 16.

measuring about 8 mm. in diameter (Fig. 10*A*). In the left axilla there was a large, firm, movable lymph node about the size of a lemon.

On July 7 the left thumb was amputated and a left axillary dissection was carried out. The microscopic examination of the specimen from the thumb amputated

posterior over the right lower quadrant. A week prior to admission a small node was removed from the scar over the femoral region. The report was positive for melanoma.

The physical examination revealed an elderly man in excellent condition for his age. The area over the right inguinal region and over the right femoral region showed operative scars and radiation effects, induration and thickening of the tissues. There were a few soft palpable nodes in the left inguinal region.

The treatment at the Memorial Hospital consisted of external irradiation using fractionated doses of high voltage x-rays and a similar plan of radium pack exposure. Two series of treatments by Coley's toxins were given intramuscularly and intravenously for a total of twenty-five injections.

A second femoral dissection was advised, but the patient decided to return to Toronto, where this operation was performed on June 24, 1935.

CASE 7.—C. A., a white male clerk, aged 30 years, applied to the Memorial Hospital on Aug. 4, 1922.

About four and one-half years prior to application, the patient observed a small black streak in the right thumb nail, which persisted and gradually increased in size to involve the entire nail. The nail finally became ulcerated. The nail was curetted but did not heal, and the lesion increased in size. Another curettage was done without improvement. In April, 1922, four months before application, the patient noticed a lump about the size of a small egg in the right axilla. This axillary tumor and the two distal phalanges of the involved thumb were removed at another institution in July, 1922. Microscopic preparations of these tumors were loaned to the Memorial Hospital, where the diagnosis of malignant melanoma was made.

On admission a small skin nodule was found near the scar of the thumb. A thickened plaque 2 by 3 cm. in diameter was present in the lower end of the linear axillary scar. A node of suspicious character could be felt high in the right axilla. It was difficult clinically to determine whether this induration and lymphadenopathy were recurrent melanotic tumors or inflammatory swellings.

The nodules on the thumb and in the axillary scar were treated by low voltage roentgen rays and by the application of small radium plaques at a distance of 1 cm.

The nodule on the thumb and the indurated plaque in the axillary scar had disappeared completely by Aug. 12, 1922, which is sufficient evidence to question the neoplastic nature of these so-called recurrences. There was no evidence of disease at the last examination on Aug. 1, 1935.

## 2. Curettement Elsewhere. With Involvement of Regional Nodes at the Time of Admission to the Memorial Hospital.—

CASE 8.—J. D., a clothes operator, aged 64 years, applied to the Memorial Hospital on June 6, 1934.

Six years prior to admission, he had pinched his left thumb in a machine, following which a black discoloration appeared under the nail and the nail came off. About three years before admission, he noticed a small granular outgrowth on the dorsal aspect of the nail bed. A biopsy was done at another hospital, with the diagnosis of "infiltrating nevocarcinoma of the melanoma type." Nine days later he received two skin units of x-ray therapy. The wound healed and the patient had no further trouble until April, 1934, when he pricked his thumb with a needle. A small granular nodule appeared which gradually increased in size. About this time he noticed a mass in the left axilla which gradually increased in size. He was referred by the hospital which had made the previous diagnosis.

### 3. *Curettement Elsewhere, With No Involvement of Regional Nodes at the Time of Admission to the Memorial Hospital.*—

CASE 11.—C. R., a male, aged 64 years, applied to the Memorial Hospital on May 28, 1935.

About ten years before this, the patient had noticed a black band involving the central subungual tissues of the right index finger. This remained static for seven or eight years, then disappeared completely. Sometime later a similar discoloration appeared at the mesial edge of the nail, involving the tip of the finger. In January, 1935, a small pigmented papillary tumor developed at the mesial edge of the nail, near the center of the previously described area. This small tumor, the size of a pea, was removed on April 1. Healing was progressive. There was no pain and no evidence of inflammation.

Examination showed that the mesial half of the nail of the right index finger had been removed. The remaining half was somewhat elevated. There was a black pigmentation of the soft tissues of the tip of the finger which extended into the subungual region. (Fig. 10B.) There was evidence of rather recent infection. There were no palpable lymph nodes in the right axilla.

On June 3 the finger was amputated at the level of the midphalangeal joint. Later, additional incision and drainage were done in order to lessen the severity of the hand infection. On July 3 the patient was discharged, to return twice a week for dressings. On Sept. 23 the hand was well healed, with excellent function. There were no palpable right axillary lymph nodes. In view of the patient's age and recent hospitalization, prophylactic axillary dissection was not done. The patient has been alive with no evidence of recurrence for two and one-half years.

CASE 12.—C. M., a physician, aged 46 years, came to the Memorial Hospital in January, 1932. At that time he was under the care of a Boston surgeon who wished an opinion. Dr. Ewing termed the biopsy an extremely low-grade but definite subungual melanoma. Amputation of the terminal phalanx was advised, but it was not done in Boston.

In 1924 the patient had noticed some discoloration of the nail which looked like a sliver. The nail was intact for about a year, then started to discharge, becoming a chronic whitlow with attacks of acute inflammation. In March, 1931, he injured his left thumb, following which some of the nail was removed. There was a second injury in June, 1932. The nail had been removed on three different occasions.

On Sept. 13, 1932, he made application to the Memorial Hospital. The examination showed a perfectly definite black recurrence in the nail bed, measuring roughly 3 by 5 mm. There was also one tiny suggestive nodule lateral to this but it was too small to be certain whether this was a recurrence. There was an enlarged node in the left midaxilla. He complained of some pains in the lower lumbar region. His general health was good.

On Sept. 13, the terminal phalanx of the left thumb was amputated. The microscopic report gave the diagnosis of melanoma. Aspiration biopsy of the axilla showed no tumor cells.

The left axilla received 58,000 mg. hours of radiation by a 4 gm. radium element pack applied at a radium skin distance of 10 cm.

In October, 1932, the nodes in the axilla were much smaller, and a year later they had disappeared and there was no evidence of disease. In November, 1934, they recurred, and a month later the patient wrote for advice regarding the axillary dissection. In January, 1935, this was done in Boston. In June, 1935, the chest was completely filled with metastatic nodules. The liver was not enlarged, and there was no evidence of metastasis other than in the chest. The date of death was not ascertained.



at the metacarpophalangeal joint showed melanoma, grade III. The microscopic examination of the axillary lymph node showed melanoma, grade III.

Both wounds healed by primary intention, and the patient was discharged in good condition on July 18, 1934. When he reported on Sept. 17 there was no evidence of disease but considerable lymphedema of the left arm. The arm could not be extended above the level of the shoulder.

On Oct. 10 the patient's physician telephoned that he was hemiplegic (a sudden vascular accident) and that his condition was critical. Word was later received of his death on that date.

CASE 9.—A. T., a man, 59 years of age, applied to the Memorial Hospital on April 15, 1930.

Three years prior to admission a chiropodist cut the nail of the great toe. This did not heal and so-called "proud flesh" had grown over the edge. He was operated upon in Germany and a skin graft was done.

On admission the end of the great toe was occupied by a tumor about 3 cm. in diameter. It bled fairly easily but was not tender. In the left inguinal region were a few rather firm nodes and a few other firm nodes running along the course of the femoral vein.

On April 16, 1930, the patient was admitted for amputation of the left great toe and excision of the tumor in the left groin. The inguinal nodes and surrounding fat were removed en masse. One node about 2 by 2 cm. in size was seen to contain metastatic melanoma. The pathologic report showed the contents of the inguinal region to be fat and fibrous tissue, at one end of which were two inguinal nodes, intensely black, fairly soft, and evidently containing metastatic melanoma.

The great toe was amputated. The pathologic report was as follows: The nail is absent. Springing from the matrix of the nail is a fungating tumor with overhanging everted margins. It is roughly divided into three distinct lobulations. The margin of the toe is surrounded by a thin border of black which is characteristic of subungual melanoma. The tumor proper is reddish gray, with one small central pigmented spot. On the medial side of the toe, 5 cm. posterior to the line of excision, is a tiny black spot firmly attached to the fascia.

On May 29, 1930, the patient was discharged in good condition. When seen in the clinic on Oct. 15 there was no evidence of disease. Death occurred in May, 1931.

CASE 10.—W. M., a white male, aged 34 years, applied to the Memorial Hospital on May 27, 1929.

Two years previously a small black spot had appeared on the nail of the right forefinger. This gradually increased until the whole nail was black. There was no pain nor any similar change in any other part of the body. His physician discovered an enlarged lymph node in the infraclavicular region and a nodule in the right chest. These were not typical of melanoma, but external radium therapy was given, with disappearance of the questionable lymph node and cutaneous nodule.

On May 15, 1930, as the disease seemed to be getting worse, amputation was advised. This was refused. The patient then went to Germany where scrapings from the blackened nail were examined microscopically and found on culture as well to contain a black pigment-producing fungus (*onychomycosis nigrescens*). On his return to the United States, bearing these cultures with him, he ridiculed the original diagnosis of subungual melanoma. The diagnosis was adhered to, however, because of the coal black line of pigment bordering the nail. Finally, he consented to amputation, and the specimen was then found to be true malignant melanoma (Fig. 4). On a clinic visit on Feb. 20, 1933, there was no evidence of disease. On June 14, 1935, the patient wrote that he was feeling well and was having no further trouble.

been perfectly normal. The bluish discoloration persisted without change in size or color until January, 1927, when it began to grow and soon became ulcerated without obvious cause. The only treatment had been the application of sundry salves to the toe.

On the outer surface of the left fourth toe, there was an elevated, ulcerated tumor, 3 by 2 by 2 cm. (Fig. 10E). This mass was soft and slightly movable on the toe. A radiograph of the foot on Aug. 16, 1927, showed atrophy of disuse, but no evidence of invasion of the bones of the foot by the tumor.

While the patient was awaiting admission to the hospital, she received one high voltage roentgen-ray treatment over the involved toe. On June 29, 1927, the fourth toe was amputated. The histologic diagnosis of the tumor by Dr. Ewing was non-pigmented melanoma, grade III. The wound healed satisfactorily. On Aug. 9, 1927, a small brown lump was noted in the center of the scar of amputation. This nodule was excised on Aug. 18, 1927. Histologic examination of this tissue showed a few pigment-bearing cells in the vessel sheaths of the derma but no definite tumor tissue. The patient was seen periodically in the clinic until April 4, 1928, during which time there was no evidence of recurrence. She was lost to observation until Nov. 5, 1928, at which time the toe stump was well healed, the general health good, but a large hard tumor was evident on the inner aspect of the left thigh.

The patient refused surgical and radiation treatment. Several new tumors appeared on the left leg. In June, 1929, these tumors were excised at another hospital. In August, 1929, the lower end of the recent incision was hard and slightly elevated by a recurrent tumor mass. In September, 1929, the scar on the thigh was surrounded by many hard subcutaneous nodules. In November, 1929, she complained of severe pain in the lumbar region. New tumor masses were evident in the left groin and popliteal space. In December, 1929, the tumors on the thigh were increasing in size and many new nodules had appeared over the entire leg. There was rapid loss of weight and strength. On Jan. 22, 1930, when last seen, the patient was bedfast and seemed to be completely paralyzed. This condition was attributed to cerebral metastases. Death occurred on Sept. 7, 1930.

CASE 16.—M. G., a white woman, 68 years of age, applied to the Memorial Hospital on Nov. 18, 1935.

About five years previously the patient had noticed a small black area on the skin bordering the nail bed of the left great toe. This became infected and she was treated at another hospital four and one-half years ago with ointments, whirl-pool baths, and lamps. The nail became markedly deformed at that time. She then went to a dermatologist who prescribed an ointment, diagnosing the disease as probable ringworm. The condition improved until about three years prior to application. She noticed that the skin on the dorsum of the toe was gradually becoming black. Two years before application she noticed a black area on the anterior and ventral surfaces of this toe, which had slightly increased in size. Five weeks prior to application she went to the clinic of another hospital. Amputation was advised, but she refused to have it done. This hospital referred her to the Memorial Hospital.

On examination, in the dorsum of the left great toe there was a black area measuring in its largest diameter 2.5 by 2.5 cm., irregular in outline, with sharply defined borders. The nail was deformed and thin in its anterior portion. In the antero-ventral surface of the great toe there was one black area 1.5 cm. and discoloration of the skin, with moderate keratinization of the central area (Fig. 10F). Situated in the dorsum of the second toe there was a small 2 mm. darkened area, in the web directly between the second and third toes another one, and in the medial ventral aspect of the arch two other small 2 mm. pigmented areas. There was no inguinal adenopathy.

CASE 13.—M. P., a Russian Jewish housewife, aged 57 years, applied to the Memorial Hospital on April 4, 1928.

In 1926, two years prior to application, the patient noticed bleeding under the right great toenail. The nail was split but not elevated. No pain was experienced at this time. The bleeding continued until the nail was partially removed and the lesion curetted at another hospital in September, 1927. On Nov. 28, 1928, the sanguineous discharge recommenced. Sudden severe pain was felt in the toe on March 16, 1928.

Under the right great toenail was an ulcerated, reddish tumor measuring 2 by 1 cm. and elevating the nail (Fig. 10C). There were no palpable nodes in the popliteal or inguinal regions. A biopsy was reported on March 13, 1928, as suggestive of melanoma.

On March 25, 1928, the great right toe was amputated at the midpoint of the first metatarsal bone. Section through the toe and lesion showed numerous granular areas, flecked with brown pigment. The microscopic diagnosis by Dr. Ewing was melanoma, grade III, radioresistant. Histologically the tumor was composed of solid sheets of cells with very few invasive tendencies. The overlying epidermis was thin and flattened by the pressure of the subjacent tumor. There was considerable lymphocytic infiltration of the stroma. The cells were large, spheroidal, and epithelioid, with granular cytoplasm, large ovoid nuclei, and well-marked nucleoli. There were very few spindle cells and infrequent areas of pigmentation.

On May 1, 1929, one large lymph node of indefinite nature was felt in the right inguinal region. An immediate treatment was given by the radium element pack. The node disappeared and there has been no further evidence in the foot or in the groin, a survival of nine and three-fourths years.

CASE 14.—A. R., a woman, 50 years of age, applied to the Memorial Hospital on July 21, 1937.

In August, 1936, the patient had scratched her finger with a piece of tin. This healed, but three or four months later she hit the same region on a gas jet. A granular structure came on the dorsum of the right forefinger just beneath the level of the nail. It was incised several times and then disappeared. It recurred about three months prior to application. It drained some pus and grew so rapidly that it involved almost the entire distal portion of the terminal phalanx of her forefinger.

The examination showed a soft, lobulated, radiating tumor of the nail bed, pushing the nail upward and forward and splitting it and extending to the distal phalangeal joint (Fig. 10D). It was smooth and apparently not ulcerated. It had many features of a pyogenic granuloma. The biopsy was reported as malignant melanoma. The lymphoid tissue in the right axilla could be palpated, but there were no discrete nodes discernible.

On Aug. 6, 1937, the right index finger was amputated at the second phalangeal joint. The wound healed satisfactorily. On Sept. 15, 1937, a right axillary dissection was performed. In the section of the fat three nodes were found, the largest of which measured 2.5 cm. in diameter. The microscopic examination showed melanoma in the peripheral sinus of one of the nodes.

On Oct. 11, 1937, the finger was well healed, and there was no evidence of disease. At the end of 1937 the patient was still reporting to the clinic.

#### 4. No Previous Surgical Treatment.—

CASE 15.—K. T., an Irish woman, aged 57 years, applied to the Memorial Hospital on June 8, 1927.

Ten years previously, in 1917, this patient had injured the fourth toe of her left foot. Soon afterward she noticed a patch of bluish discoloration, 0.5 cm. in diameter, in the region of the nail sulcus. She insisted that prior to the injury the toe had

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Amputation was advised and the condition explained to the patient's daughter. The patient refused to consider amputation. However, later she consented and amputation was done in May, 1936. There is no evidence of recurrence either locally or in the groin. The liver is still slightly enlarged. The patient is still being followed.

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# ANGIOMATOUS TUMORS OF THE HANDS AND FEET

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THE term angioma is here used to include all those tumors arising from blood and lymphatic vessels and the various components which go to make up these structures. While angiomatous tumors are not strictly limited to the extremities, certain members of this group, such as the angiomoneuromas, are rarely found elsewhere, and in Kaposi's hemorrhagic skin sarcoma the initial lesion is most frequently found on the extremities.

The nomenclature of angiomatous tumors is confusing, and in the past there has existed considerable difference of opinion as to the method of classification of these tumors. In the older literature a confusion of terms has grown up, many of which do not represent clinical or pathologic entities. On the other hand, any classification may be unsatisfactory since there is frequent difficulty in reconciling the clinical course of some of these tumors with their histopathology. Some of the obvious clinical features of these tumors may not be manifest in a classification based strictly on histopathology. Such, for instance, are the difficulties encountered in attempting to explain the difference in appearance, rate of growth, character of pain, and metastasis in angiomias presenting very similar microscopic pictures.

## I. Angiomas

### a. Vascular malformations

1. Arteriovenous fistulas
2. Telangiectasis (port-wine stain, hemangioma simplex, vascular naevi)
3. Angioma (venous, arterial, lymphatic)

### b. Angioblastomas

1. Hemangioblastomas
2. Lymphangioblastomas

## II. Angiomoneuromas (glomus)

## III. Kaposi's disease (idiopathic multiple hemorrhagic sarcoma)

The multiple etiologic factors in vascular tumors are again confusing, particularly the tissue of origin. This is illustrated by the difference of opinion among the pathologists as to what should or should

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not be called an endothelioma. The vast majority of vascular tumors are congenital, or at least the anlage is present early in life, even though the tumor may not become manifest until old age. It is frequently difficult, therefore, to determine whether trauma is a primary or secondary factor in the etiology.

Angiomatous tumors may be classed under three main divisions. The first group, the angiomas, is composed of angiomatous malformations and angioblastomas. The angiomatous malformations include a variety of conditions, both congenital and acquired, in which it appears that intravascular pressure and local changes in the vascular wall play a paramount role and in which there is little evidence of true neoplastic tissue. The angioblastomas include those tumors made up chiefly of masses of angioblastic cells undergoing rapid proliferation and which appear to be true neoplasms. Mechanical factors may also play a role in this group in determining the size and progress of the tumor. The second group of angiomyxoneuromas is composed of those tumors having a specific histology, as the name implies, and arising from a specific and now well-recognized structure, the glomus. The third group, Kaposi's hemorrhagic skin sarcoma, is included among the vascular tumors with some misgivings, since its etiology is unknown. However, the tumors seem to be composed chiefly of vascular tissue.

Angiomatous tumors, with the exception of Kaposi's hemorrhagic skin sarcoma, are of importance chiefly because of the symptoms they produce, rather than because of danger of malignant change. The question as to whether the term malignant may be applied to angioma has been much discussed. Many of these tumors are locally invasive, eroding through bone, and when vital structures are involved they may result in death. This, however, only rarely occurs in the extremities, and then usually in infants and associated with secondary infection. There has also been much discussion as to whether these tumors take on malignant features from the standpoint of remote metastases. Isolated case reports (Borrmann, Sherman, Ewing, Langhans, Wright) have appeared from time to time in the older literature, the majority of these tumors having occurred in the internal organs. In many of the earlier case reports it seems quite likely that the tumors are not strictly of angiomatous origin. Metastatic tumors of the thyroid and kidney, as well as non-pigmented malignant melanomas and adenocystic basal cell cancers, have been mistaken for angioblastomas. However, there seem to be a few isolated authentic cases of metastasizing angioblastomas occurring on the extremities (Ward and Jonas).

There have been a number of sarcomas reported (Speciale) as arising from the sheaths of blood vessels, several of which have occurred in the extremity. There is also a large group of tumors under the

classification of endothelioma without angiomatous features. Because the histogenesis of these two groups of tumors is still not clearly established, they are not included in this paper.

#### ANGIOMA

The term angioma includes a variety of vascular alterations, many of which present few if any characteristics which would class them as neoplasms. In the present discussion we have divided the angiomas into two groups: (1) those which may be considered as vascular malformations, and (2) those which may be considered as true neoplasms. The latter we have designated as angioblastomas.

In Geschickter's review of 300 cases of angiomas of the skin including all types, one-third were found in children under 10 years of age and of these 80 per cent were under 5 years. This age distribution fully emphasizes the importance of the congenital origin of many of these tumors. Nearly one-third of the angiomas of the skin appear on the extremities.

*Vascular Malformations.*—Certain anatomic and physiologic observations have yielded information which is of value in explaining some of the vascular malformations. Sabin has pointed out that the primitive vascular anlage is laid down in solid cords of angioblastic cells. An apparent liquefaction then takes place in which there develop spaces filled with plasma. These later develop into minute vessels or capillaries. The Swiss anatomist Aeby in 1868 expressed the opinion that the vascular system early in its development existed as a uniform capillary network of vessels. This idea was strongly opposed until injection methods finally established the essential truth of the statement. Evans has pointed out that the larger vessels come into existence only by the enlargement of certain fortuitously situated capillaries which assume a larger and larger function and develop into arteries at the expense of other capillaries which accordingly must regress. There are, however, other methods of development by branches from embryonic arteries and in the large organs Mall has demonstrated the development of a vascular system from the so-called sinusoids.

Thoma and other investigators have demonstrated that the size of a vessel and the thickness of its wall are dependent on the rate of flow and the intravascular pressure respectively. He states: "The increase in the size of the lumen of the vessel or what is the same thing, the increase in the surface of the vessel wall, depends on the rate of the blood current. The surface of a vessel wall ceases to grow when the blood current acquires a definite rate. The vessel increases in size when this rate is exceeded, becomes smaller when the blood stream is slowed and disappears when it is finally arrested." "A second histomechanical principle may be added to this, viz., the growth in the thickness of the wall is dependent upon its tension. Further, the

tension of the wall is dependent upon the diameter of the lumen of the vessel and upon the blood pressure." These observations have been elaborated by others by the transplantation of segments of an artery into a vein and vice versa. It has been found that the transplanted segment takes on the characteristics of the vessel into which it has been transplanted. This observation is of importance in consideration of the many arguments as to whether a given angioma has arisen from an artery or a vein. Another, but less well understood, structure which may play an important role in angiomas is the arteriovenous anastomosis, the development of which has been described by Clark and co-workers.

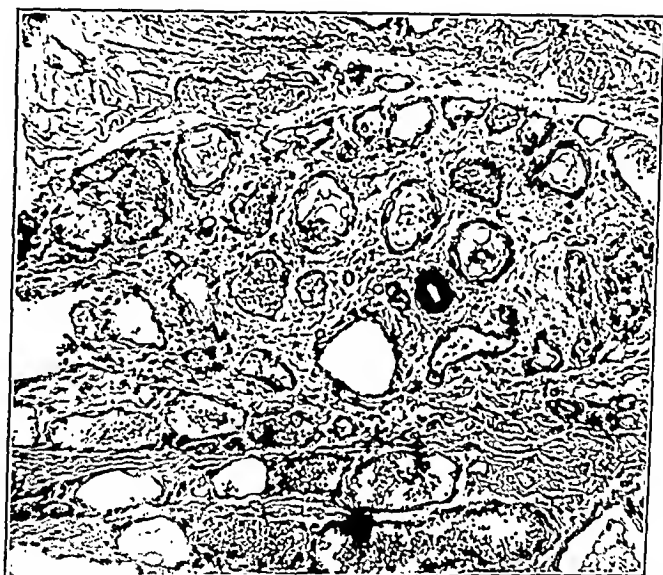


Fig. 1.—Angioma (vascular malformation) composed of numerous endothelial lined spaces in a loose connective tissue stroma without evidence of angioblastic proliferation ( $\times 100$ ), hematoxylin and eosin.

The above observations indicate some of the factors at work in the development of the normal vascular system, and unquestionably play an important role in the development of these angiomatous malformations. It is not clear whether a simple vascular malformation may develop later into an angioblastoma, but the evidence would indicate that such a transformation may occur.

Congenital arteriovenous fistulas are formed of fairly well developed arteries and veins, but frequently associated abnormalities of the various layers of the walls of the vessels are found. These are characterized by nodular overgrowth of the intima, imperfect formation of the media with a tendency to form leiomyomatous nodules and aneurysmal outpocketings. While such angiomas may develop rapidly,

forming large tumors, there seem to be no other characteristics suggesting that they are true neoplasms. Obliteration of the arteriovenous opening or thrombosis of the vessels will result in a cure, although the number of intercommunications may be so great as to render this a major surgical procedure, or impossible. Reid, Holman, and others have emphasized the need for early intervention and have pointed out the likelihood of cardiac damage.

Occasionally such arteriovenous communications are seen in their simplest form, as the so-called "spider naevus" appearing on the skin. Pressure with a glass slide will reveal the minute central artery feed-

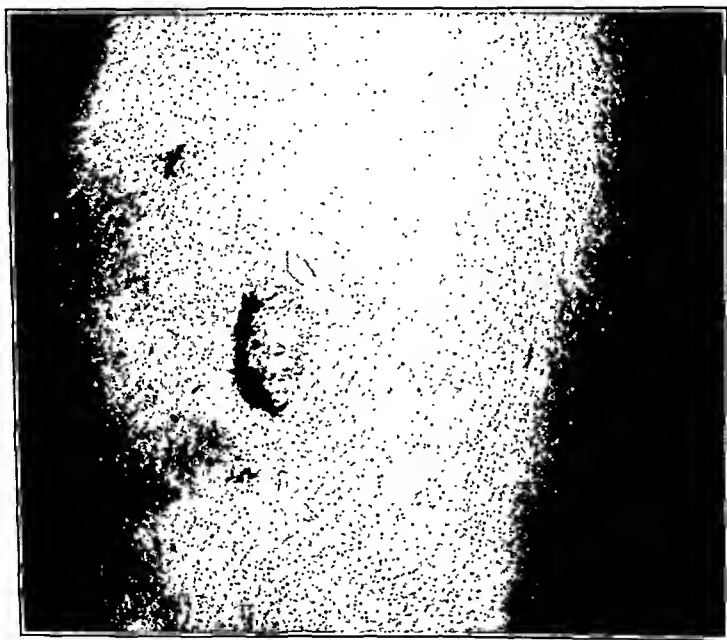


Fig. 2.—lymphangioma of leg showing site of operative drainage through which an abundance of lymph escaped.

ing the surrounding venules. These frequently disappear spontaneously, presumably by thrombosis, or they may develop into angioma. When seen in their early stages, obliteration of the small central artery by any means will result in a cure. Another group of angiomas is composed of what appear to be veins. They enlarge very slowly, usually in the subcutaneous tissues, presenting a bluish appearance. Occasionally they are painful. The port-wine stain or telangiectasis presents another of these vascular malformations. It is composed of masses of dilated capillaries with no evidences of proliferation.

Malformations of the lymph vessels similar to those seen in blood vessels are described. These lymph vessel malformations appear to be rare on the extremities. The following is an illustrative case report:

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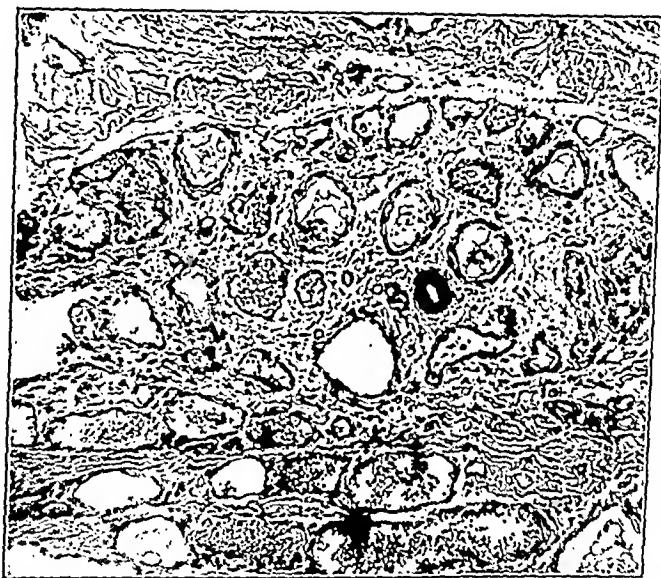


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*Angioblastoma.*—Sabin has studied the manner in which angioblastic cells are differentiated from the mesoderm and how following proliferation solid cords of angioblastic cells are formed. Liquefaction takes place within these masses of cells so that a space filled with clear plasma is formed and lined by endothelium from the angioblastic cells. With this process in mind it is readily seen why some of the angiomas are chiefly made up of solid masses of angioblastic cells and why there may be a varying number of capillary, cavernous, or cystic spaces. It also explains why in the treatment of such tumors obliteration of the vascular channels may not be nearly as successful in producing a cure as in the former type.



Fig. 4.—Lymphangioma of leg showing widely dilated endothelial lined spaces extending into the corium with no evidence of angioblastic proliferation.

These tumors may consist of numerous capillary or cavernous spaces with varying amounts of angioblastic cell proliferation. In other instances this proliferation predominates with masses of these cells and few vascular channels. Numerous cells in mitosis may be found indicating the active growth. This new growth extends and infiltrates the surrounding tissue and frequently compresses the vessels of the normal tissue. Because of the great variation in histologic structure, a multitude of names has been used to designate the types. These tumors have been called capillary or cavernous hemangioma, angiosarcomas, endotheliomas, etc. The most common of these histologic

CASE 1.—W. Y. (No. 62552), a 14-year-old boy, entered the New Haven Hospital Aug. 7, 1938, complaining of a swelling on the medial aspect of the left thigh of ten years' duration. At the age of 4 years, he had had poliomyelitis and while in the hospital a swelling appeared on the left thigh just above the knee—which was mistaken for an abscess and incised, but only clear fluid was obtained. Since that time the tumor had slowly grown larger. The scar had developed a marked keloid and at intervals would break down and a considerable quantity of clear fluid would drain. Physical examination revealed a doughy tumor of indefinite outline, 6 inches in diameter.

The overlying skin had the appearance of an ill-defined port-wine stain on which there was an increased hair growth. At operation the tumor with the overlying

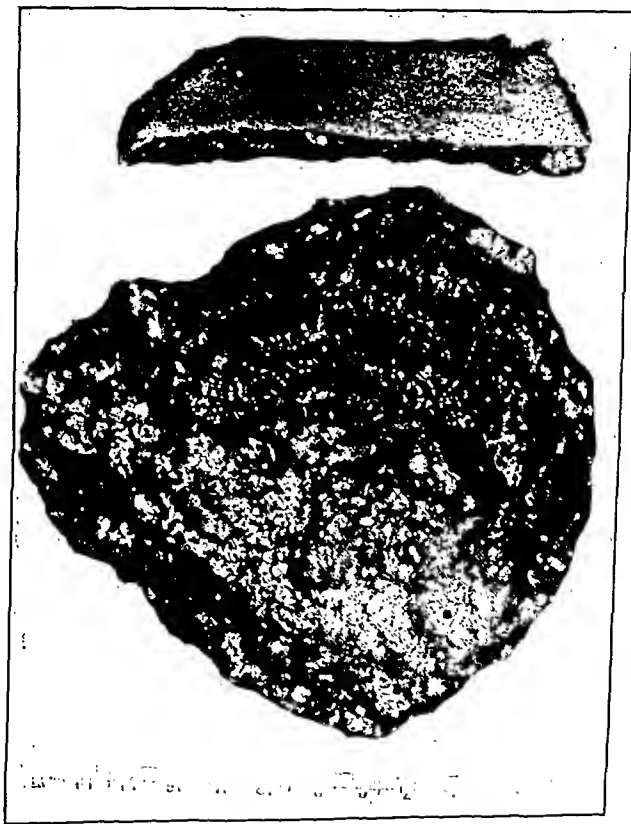


Fig. 3.—Lymphangioma of leg. Operative specimen showing large lymphatic spaces in the subcutaneous fatty tissue.

skin was excised. There was difficulty in distinguishing the limitations of the tumor from the surrounding fat, which could best be done by the difference in the consistency of the tissue when cut as the tumor was traversed by very fibrous trabeculae. The tumor extended down to but did not penetrate the deep fascia. The tumor had a rich blood supply and was made up of large spaces filled with clear fluid between fibrous trabeculae. Microscopically, it was composed of numerous endothelial lined spaces of varying size embedded in a dense acellular connective tissue. The tumor extended into the corium directly beneath the epithelium. In none of the sections was there evidence of angioblastic proliferation.

*Hemangioma of Skeletal Muscles.*—Among the tumors occurring in the deeper structures of the extremities, and particularly in skeletal muscles, are hemangiomas. Because of their frequency and need for clinical differentiation, they are considered separately, although they in no way differ from angiomas elsewhere. Nearly 300 such tumors now have been described in the literature, approximately two-thirds of which have occurred in the extremities. They are nearly twice as common in the lower extremity as in the upper. They are more likely to be found in the larger muscles of the upper arm, thigh, and calf, but they have been reported as occurring even in the small muscles of the hand. The etiology of these tumors is not clear, but it is the consensus of opinion that the majority of them are probably congenital. They are more frequently encountered in the second and third decades of life, and nearly 95 per cent of all the tumors have been reported in patients under 30 years of age. The importance of trauma as an etiologic agent is open to question. There have been some cases reported in the literature (Mailer) which suggest that the tumor may have followed the trauma, but, on the other hand, there is always the possibility that there was a small tumor preexisting and the enlargement may have been due to hemorrhage following trauma.

*Pathology.*—The tumors are usually round or ovoid, varying in size from less than one to several centimeters in diameter. The histologic picture varies greatly, as it does in hemangiomas elsewhere. For the most part they are composed of rather large blood spaces with an endothelial lining and rather loose fibrous tissue. In some instances there may be such a marked proliferation of fibrous tissue as to lead easily to a diagnosis of sarcoma. However, they do not metastasize, and it is likely that the few instances of recurrence (6 per cent) have been due to incomplete removal.

*Clinical Features.*—The majority of these tumors are undiagnosed before operation. They are usually 4 to 5 cm. in diameter, situated deeply in the muscle. Some of the tumors are soft and compressible, while others are firm. Only rarely has the tumor been adherent to the skin. A considerable number have shown phleboliths on x-ray examination. Spontaneous pain is unusual, although there may be pain and soreness associated with exercise. In the larger tumors there may be limitation of movement and some loss of function. If the tumors are adjacent to the larger vessels or nerves, there may be atrophic changes. Occasionally there is a discoloration of the skin, sometimes dilated veins, and sometimes bruit.

*Treatment.*—The treatment of these tumors is surgical excision. Frequently the tumor infiltrates between the muscle fibers, which undergo degeneration, and it may be necessary to sacrifice a considerable portion of the muscle involved. While these tumors rarely if ever become malignant, they may increase in size, making total removal still more



varieties among the peripheral hemangiomas is the capillary type (Geschickter). In spite of the apparent malignant appearance of many of these tumors, it is rare for them to develop metastases and only by their local infiltrative growth do they destroy tissue or interfere with function of a part.

The treatment of angioblastomas of the extremities is similar to that employed for angioblastomas elsewhere. The best cosmetic results can be obtained by surgery if the tumor is small and the surrounding tissue loose. On the other hand, good results can be obtained by radiation, although on the extremities the effect of radiation on the surrounding normal vessels deserves more consideration than when the

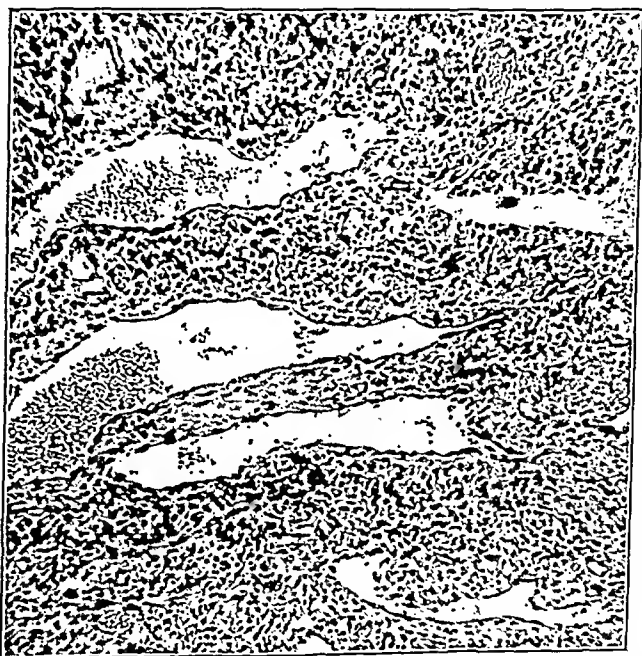


Fig. 5.—Angioblastoma. Note extensive angioblastic proliferation between vascular channels forming solid cords of cells in many places ( $\times 100$ ), hematoxylin and eosin.

tumor is situated on the trunk. Sclerosing solutions also may be used successfully.

Lymphatic vessels may be the site of origin of angioblastomas. These usually consist of congeries of lymph vessels which tend to be dilated and which may form large cysts. Proliferation of the angioblastic cells as well as of lymph vessels may occur, although it is uncommon for this angioblastic cell proliferation to compose the major part of the tumor as is frequently seen in the hemangioblastomas. Malignant lymphangioblastomas are so rare that as Stout states: "There are many pathologists who have never seen (or at least never recognized) one."

*Brief Review of the Literature.*—The modern literature on glomus tumors dates from the observations of Barre (1920-1922), a French neurologist, and Masson, 1924, a French pathologist. However, it is evident that these tumors were recognized as clinical entities at a much earlier date, although under different names. As is frequently true, it is difficult to determine who first recognized these small, painful subcutaneous tumors as a clinical entity. The term "painful subcutaneous tubercle" was used by William Wood, of Edinburgh, in 1812 in describing a clinical syndrome which he had observed as well as collecting several cases from the literature. His description clearly indicates that most if not all of these cases of "painful subcutaneous tubercles" were angiomyxoneuromas. However, only one of his cases occurred on the finger. Numerous other surgeons previous to this time were undoubtedly familiar with this small, painful tumor, among whom may be mentioned Campes, 1760; Morgagni, 1762; Cheselden, 1788; Bisset, 1792; Antoine Petit, 1799; and Dupuytren, 1835. With the advent of histopathology, further reports appeared (Kolaczek, 1877; Kraske, 1880; and others) and during this period they were usually classed as angiosarcomas. Muller in 1901 changed the name to "perithelioma" and Batigne and Gaudy (1901) to "fibromyxomatous angioma." Other similar reports followed indicating that the tumor was being recognized as not a true sarcoma.

Barre in 1920 reported a case of a bluish tumor occurring underneath the finger nail associated with severe paroxysms of pain radiating up the arm to the neck and right side, associated with a Horner's syndrome and changes in the vasomotor reflexes. Excision of the tumor gave complete relief of symptoms. Barre gave this tumor, as well as others observed later, to Masson for study. Masson had obtained a similar subungual tumor in 1916. Stout summarizes his observation as follows: "He was struck by the fact that all three tumors had the same morphology and that all the patients had suffered from paroxysms of pain. He noted that the tumors were made up of a tangled mass of well developed arterioles, some with smooth muscle in their walls, all of which had peculiar 'epithelioid' cells arranged about their lumens. Moreover, the supporting framework of the tumors contained large numbers of nonmyelinated nerves, some of which were directly continuous with the cytoplasm of the epithelioid cells. All three tumors had large corpuscles of Vater-Pacini compressed and flattened out against their capsules, and these Masson felt must have been responsible for the pain. Believing that such a growth must represent the hypertrophy of some sort of an organ, because of its orderly arrangement and rich nervous connections, he examined serial sections of fingers, and came upon peculiar arteriovenous anastomoses which exactly resembled the structure of the tumors. These were found everywhere in the deeper layers of the skin of the

difficult; hence early excision is indicated. It is important to recognize that these tumors occasionally may grossly and microscopically simulate sarcoma, and amputation has been needlessly performed.

*Angioma of Bones, Joints, and Tendons.*—Angiomas are among the less common bone tumors, and, while a considerable number are reported in the older literature, many of them were not true angiomas. The tumors are most frequently found in the second and third decades of life, although several have been reported in children. Frequently there is a history of preceding trauma. In the extremities they are usually near the ends of the long bones, although they have been seen in the midshaft. They are usually accompanied by a history of pain. There may or may not be a palpable tumor, and occasionally they have been described as soft or pulsating. The roentgenogram characteristically gives a multilocular or soap-bubble appearance with an expanding shell of paper thinness. Observation for a period may reveal that the tumor is extending in one direction only. The majority of these tumors have been described as cavernous, with little or no angioblastic tissue.

While these tumors are almost without exception nonmalignant, they, nevertheless, require treatment because of local extension and destruction of bone. They are usually successfully treated by curettage, cautery, or radiation.

Lymphangiomas and hemangiomas occur in and about joints and in tendon sheaths. These tumors may be congenital or may follow trauma. Occasionally these tumors are bilateral, indicating their congenital origin. They are usually accompanied by pain and boggy swelling, and the hemangioma occasionally pulsates. Some of these tumors following trauma are associated with a throbbing pain and vasomotor disturbances. Occasionally they may disappear spontaneously, presumably by thrombosis. The authors have seen one case in which the tumor followed a traumatic injury to the wrist. At operation profuse hemorrhage was encountered so that the removal of the tumor was given up. Following this the tumor disappeared, but the pain and vasomotor phenomena persisted and were relieved by a dorsal sympathectomy. The lymphangiomas of tendon sheaths and joints should be distinguished from degenerative cysts arising from the synovial membranes. The erosion of bone cannot be taken as evidence of neoplastic tissue, since the same phenomena may be observed in aneurysms and glomus tumor. The majority of these tumors would seem to fall into the group of angiomatous malformations.

#### ANGIOMYONEUROMA

This remarkable tumor has been recognized only in recent years and, owing to its unique histopathology, the severity of the symptoms and the physiologic importance of the glomus, it deserves special consideration.

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fingers, and in greatest numbers where the tactile corpuseles of Wagner-Meissner were present in the papillae. Somewhat similar structures had been described by Ruffini but without all the details noted by Masson, who could not be sure, therefore, that they were the same. Since this structure was a glomus (i.e., a conglomeration or plexus of minute arteries or veins) he felt it should have a distinguishing descriptive term and therefore called it a neuromyo-arterial glomus."

Since this time an increasing number of reports have appeared in the literature from all parts of the world, indicating that the tumor is probably of even greater frequency than at first supposed.

*Arteriovenous Anastomosis. The Normal Glomus.*—The histopathologic studies carried on by Masson and his associate, Popoff, have led to

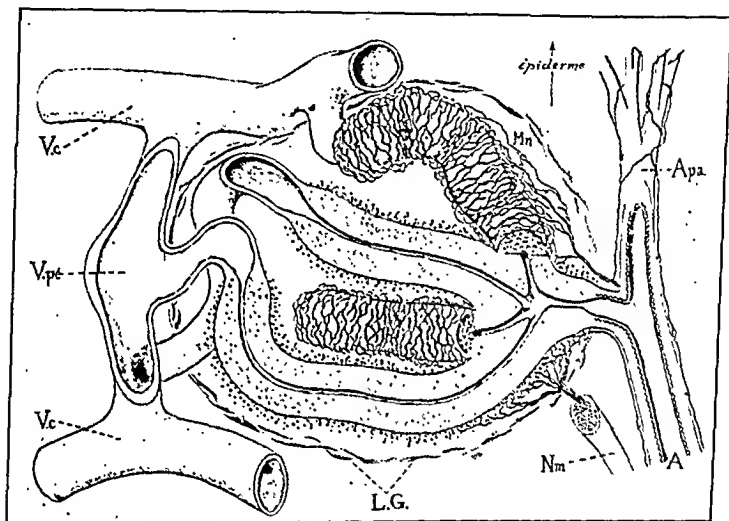


Fig. 6.—Schematic reconstruction of a glomus. A, Superficial preterminal artery. Apa, Terminal branch entering capillaries. L, The side branch is the afferent artery entering the glomus dividing into four neuromuscular arterioles. The elastica of the afferent arteriole disappears as soon as the arteriole enters the glomus. The wall of the vessel becomes thick due to an increase in smooth muscle fibers which terminate abruptly with the beginning of the venous segment. The efferent glomic vein leads into a collecting vein (Vpt) which is dilated and thickened at the junction and in turn leads into the superficial veins, Vc. Mn is the rich perivascular network of nerves showing connections with the periarterial sympathetic nerves as well as myelinated sensory nerves to the skin. (After Masson.)

a renewed interest in the normally occurring arteriovenous anastomoses. The long-established concept that the blood normally passes from the arterioles to the capillaries to the venules has been so well established that it has been difficult to conceive of another normal means of communication between the arterial and venous systems. Nevertheless, as in the instance of the glomus tumors themselves, the existence of such a communication has long been known.

Müller in 1844 described direct connections between the arteries and cavernous sinuses of the penis. Subsequently, in 1862, he described direct connections between the arteries and veins of man in various

parts of the body. In 1877, Hoyer published a paper on "direct openings of very small arteries into vessels of venous character." Similar observations were made by Bourceret in 1855 and by Gerard in 1895 when the term arteriovenous anastomosis first appeared. A classical description of the histology of these anastomoses has been given by Grosser (1902). Space does not permit more detailed review of the numerous investigations of these interesting structures; for it the reader is referred to the excellent review by Eliot R. Clark. Arteriovenous anastomoses remained of academic interest until the work of Masson, since which time they have attracted the attention of physiologist, pathologist, and clinician. Masson linked the normally present arteriovenous anastomosis for the first time with a pathologic condition. In recent years several physiologists have studied the normal activity of these structures in the living animal. In 1930 Grant published his observations on arteriovenous anastomoses in the intact ear of living rabbits. He found that on heating the ear the arteries dilated at  $35^{\circ}$  C. and the arteriovenous anastomoses dilated at  $40^{\circ}$  C. He concluded that these structures are important in regulating body temperature. Clark, using a double-walled window in the rabbit's ear, has studied the activity and development of the arteriovenous anastomoses over a long period of time. He found that they exist in great numbers, twenty-five to fifty per square centimeter, and that their number may be greatly increased by exposure to trauma, temperature changes, or inflammation. In general, they behave in much the same way as arterioles, the chief difference being one of degree, for they are decidedly more active and show a greater tendency to independent action. "So rapid is the action of the arteriovenous anastomosis that it resembles a rapidly-acting stopcock." Clark states: "Regarding the function of arteriovenous anastomoses, the most one can say definitely is that, when dilated, they permit a large amount of blood to pass from artery to vein without passing through the capillaries. They undoubtedly play a part in the surface heating or cooling of the blood in the human hand and forearm and in the rabbit's ear, since they must allow a greater total flow through the exposed veins than would be possible without them."

*Histopathology of Tumor.*—The histopathology of the classical tumor is remarkably consistent. However, Clark has demonstrated the development of new arteriovenous anastomoses in the living animal and others have also shown great variations of these structures in fixed specimens. It is therefore not surprising that painful tumors composed of blood vessels which do not conform to the classical description are frequently found. The following description of the histology of the classical tumor is taken from Stout:

"The glomic tumors are composed of a tangled mass of blood vessels enclosed within a capsule. These vessels are lined with a single layer

of endothelial cells which are sometimes flattened and sometimes swollen. The endothelial layer is supported by a fibrous layer which may be quite thick but is usually exceedingly delicate, so that it can be seen only with silver or other differential fibrous tissue stains. The rest of the wall varies considerably in thickness and is made up of the peculiar cuboid or rounded 'glomus' cells (usually referred to as 'epithelioid' cells because Masson so described them) and smooth muscle, either well differentiated or in an embryonal form, in which the smooth muscle fibers are found within the cytoplasm of the epithelioid cells.

"The smooth muscle in some of the vessels, particularly those near the periphery of the tumors, is not infrequently in distinct bundles, which sometimes run parallel with the long axis of the vessel and sometimes tangential to it, but rarely completely surround its lumen. Usually there are epithelioid cells in the gap where the muscle is missing, and often there are epithelioid cells external, or internal, or both external and internal to the muscle bundles. Masson believes the vessels that are well provided with muscle are afferent to the glomus. The majority of the vessels, however, have no recognizable smooth muscle fibers either differentiated or undifferentiated.

"The glomus cells are quite distinctive. They have well defined cell outlines which are further accentuated by the presence of delicate collagen fibers which separate every cell from its neighbor. The cell cytoplasm is pale, amphophilic, and sometimes vacuolated, which brings into sharp relief the voluminous, centrally placed, globular or ovoid nucleus. It is a rare event to find a mitotic figure. Some of the glomus cells have short smooth muscle fibers within their cytoplasm.

"In the subungual tumors most of the vessels have small lumens containing rare erythrocytes. Outside of the nail bed the caliber of the tumor vessels may vary greatly, and some have dilated lumens similar to those seen in cavernous hemangiomas.

"The collagen fibers which form a meshwork between the epithelioid cells pass outward to join the stroma of the tumor which lies between the vascular complexes. This stroma is generally loose-textured and often shows mucinous degeneration (demonstrated by the mucicarmine stain).

"There are generally bundles of myelinated nerves in or near the capsule of the tumor which are recognizable with any stain. In addition, Stout has demonstrated, by the Gros and Rogers technique, the presence of numerous slender nerve fibers, seemingly without myelin sheaths, beneath the capsule especially and to a less extent in the stroma of the tumors. These fibers pass among the epithelioid cells which both Masson and Mason and Weil have shown are in direct continuity with the cytoplasm of these cells."

*Clinical Features.*—The distribution of angio-myoneuromas is almost entirely limited to the extremities, although an occasional case has

been reported on the trunk. Approximately two-thirds of the cases have been found in the upper extremity and one-third in the lower extremity. About one-third of the tumors have been subungual and nearly one-half of them have occurred in the digits.

The age of onset of the tumors varies from childhood to old age. The average age at which treatment is sought is in the third decade. The duration of the tumors varies enormously, from a few weeks to as long as thirty-seven years. This great variation in the duration is apparently dependent on the severity of pain and the ease with which a diagnosis is established.

The outstanding symptom associated with this tumor is pain. The occasional nonpainful tumor has been removed. Some of these tumors (Picard) do not develop spontaneous pain over long periods but are manifest merely as areas of increased sensitivity. The pain in the classical case is described as exquisite, agonizing, burning, throbbing, or bursting. The pain frequently occurs in paroxysms which may be initiated by pressure, changes in the weather, posture, or hot or cold water. At times there seems to be no reason for the paroxysms of pain. In some patients the pain may be so severe (see Case 2) and the radiation of pain so extensive that the localizing signs or trigger-point may be overlooked. The patient may wear a bandage or glove for protection, or in other instances the slightest pressure from clothing cannot be tolerated. Some patients obtain relief from pain by immersing the hand in ice water, while with others heat seems to be effective. Certain tumors may be emptied by slow pressure (Mason and Weil), following which there may be a disappearance of pain for hours. When the tumor is subungual, the patient may not allow the finger nails to be cut so that they grow to great lengths. Whether owing to the severity of the pain or associated vasomotor phenomena, sudden, unexpected trauma may result in an attack of fainting. The cause of the severe pain is obscure and, while it has been attributed to pressure on the pain body or adjacent nerve endings, a similar severe pain has been reported in arteriovenous fistulas (Livingston) without tumor formation. There are many instances of intractable pain having the same characteristics following trauma to the fingers in which no tumor could be found and amputation was the only treatment which yielded relief. Not infrequently these unfortunate patients are classed as various types of psychoneuroses and the problem deserves careful consideration from the standpoint of compensation. Changes in blood pressure frequently produce striking differences in pain. Relief may be obtained from elevation of the extremity or, if the blood pressure cuff is raised to diastolic pressure, there may be a great increase in the throbbing pain. On the other hand, if the veins of the extremity are emptied and the pressure abruptly raised above the systolic level, there may be an instantaneous relief of pain. There



is no conclusive evidence as to the pathways over which the pain is carried. Novocain block of the sensory nerves and of the sympathetic chain as well as periarterial sympathectomy have been done with only incomplete relief or change in the character of the pain. Radiation therapy is ineffective (Adams, Stabius, and others) and even after complete excision local sensitivity may remain for long periods before it finally disappears.

The signs associated with angiomyloneuromas are variable depending on the location, size, and depth of the tumor. Local tenderness is the most consistently present sign. The degree of color in the tumor depends on its size and depth. Usually a change in color is discernible and frequently it is marked. The majority of the tumors are described as blue or purplish and a few are red. Others exhibit color changes associated with vasomotor phenomena. The subungual tumors may or may not exhibit a color change as seen through the nail and frequently exist for years with no discernible color changes of the nail other than a very faint cyanosis. Inasmuch as the bulk of these tumors is usually composed of blood vessels, they frequently are not palpable unless located superficially. The size of the average tumor varies from 3 to 5 mm. and only rarely have tumors 2 to 3 cm. been reported.

Roentgenographic examination of the tumor is always worth while, particularly when the tumor is adjacent to bone. The tumor, because of its pulsatile character when in contact with bone, frequently erodes through the cortex in the manner of an aneurysm. A recent report of Bergstrand, of Stockholm, suggests the possibility of the origin of some of the tumors within bone, although this is not definitely established.

Vasomotor phenomena may or may not be associated with these tumors. Those tumors arising in the digits seem more likely to be associated with sympathetic nervous system manifestations. As a rule the involved extremity is distinctly warmer than the normal side. It has also been shown (Stabius) that recovery from exposure to cold is more prompt in such an extremity. These changes are not limited to the involved digit but involve the entire extremity and may extend to the trunk and face as unilateral sweating. Occasionally in the more painful variety a unilateral Horner's syndrome is seen, usually manifest during a paroxysm of pain. There may also be other associated reflex changes. In severe cases of long duration these phenomena may persist for months or years after removal. An increase in the pulsation of the palpable arteries may be discernible which is best demonstrated by oscillometric readings and which may be as much as double the normal extremity.

A variety of atrophic changes may be demonstrable in the involved extremity and may lead to a mistaken diagnosis of a central nervous system lesion (see Case 2). These atrophic phenomena may be brought

about by the atrophy of disuse and vasomotor changes, or both. Atrophy of the musculature seems to be chiefly a disuse phenomenon. Skeletal postural changes may result from carrying the extremity in a certain position in order to obtain relief from the pain. A soft, wrinkled, thin skin associated with the extreme hyperhidrosis may be present. In the subungual tumors the nail may be curved and thickened with longitudinal striations associated with slow growth, probably owing to interference with the nail matrix. In cases of long duration these changes may be permanent or require years for their disappearance.

*Differential Diagnosis.*—It has been previously stated that pain (induced or spontaneous) and local tenderness are the most constant symptoms of angiomyoneuroma. Other tumors occurring in the nail bed, owing to the close association with the great number of nerve endings in this region as well as the fact that it is a semiclosed space, may give similar symptoms. This suggests that the peculiar vasomotor phenomena associated with the angiomyoneuromas may not be due primarily to these tumors but to their location and associated nerve structures. However, the diagnosis of other similar tumors occurring in the literature, such as fibroma, etc., previous to the clinical-pathologic demonstrations of Masson, should be regarded with suspicion.

*Fibroma.*—Certain cases of fibrous tissue tumors have been reported (Dubring, Chandelux) which have had similar clinical features.

*Angioma.*—Occasionally cases are encountered presenting the clinical features of angiomyoneuromas which on removal fail to show all the typical features of the glomic structure. It is possible that these are similar tumors which for various reasons (incomplete development or technical) fail to show the classical structures.

*Exostosis.*—These are not infrequently painful and sometimes discolored. The roentgenogram readily yields the diagnosis.

*Sarcoma.*—While many of the sarcomas in the older literature have undoubtedly been angiomyoneuromas, true sarcomas occasionally occur.

*Carcinoma.*—The subungual carcinoma is rare, but a few cases have been reported.

*Melanoblastoma.*—The differential diagnosis of a tumor appearing underneath the nail must include malignant melanoma; first, because of the extreme importance of an early diagnosis and radical treatment; and second, because it is one of the common subungual tumors. These may follow injury and occasionally are painful, but usually the pain is a minor symptom. Ulceration is more common and pigmentation a more striking feature.

Other lesions which should be considered are subungual corns, papillomas, enchondromas, angiokeratomas, and Boeck's sarcoid.

*Angiomatous Leiomyoma.*—Solitary cutaneous and subcutaneous leiomyomas should be mentioned among the vascular tumors of the ex-

tremity; first, because some of them certainly arise from the smooth muscle of blood vessels; and second, because they may simulate the painful syndrome of the glomus tumor and have been included with these tumors in the older literature under the term "painful subcutaneous tubercle." Stont has presented an excellent review of these tumors to which the reader is referred for details.

The frequency of these tumors appears to be about the same as the angiomyonuromas, as nearly one hundred cases have been reported. The leiomyomas, unlike the angiomyonuromas, do not seem to be associated with any particular structure and may arise from smooth muscle anywhere in the skin and subcutaneous tissue. It is frequently difficult or impossible to determine their exact origin, but it is likely that nearly one-half of them arise from the smooth muscle of blood vessels. There has been considerable discussion as to whether they arise from arteries or veins and there are no tumors reported arising in the larger arteries. It seems remarkable that they should arise only in the veins, but such seems to be the weight of evidence. Nearly one-half of the tumors occur on the extremities, particularly the extensor surfaces. Unlike the glomus tumor, they are relatively uncommon on the digits and occur with greater frequency in the legs.

The clinical appearance and behavior of some of these tumors may be very similar to the angiomyonuroma. They are usually of small size (2 to 15 mm.), although, unlike the glomus, they may reach several centimeters in diameter. Occasionally the tumor is pedunculated, but usually it is in or underneath the skin. The tumor is usually colorless but occasionally has been described as varying shades of brown or red, and in a few instances as bluish. The tumor usually is painful or tender (twelve of fifteen, according to Stont). Occasionally the pain may be paroxysmal in character with radiation similar to that in the glomus tumor. However, as a rule, the pain is less severe and less likely to be paroxysmal in character. The cause and mechanism of the pain are not clearly established. However, contraction or wormlike movements have been observed during a paroxysm of pain and some tumors have been seen to contract after removal. These tumors occasionally undergo malignant change with metastasis to lymph nodes, bone, and viscera. A history of preceding trauma is sometimes obtained, but there seems to be no established relationship between trauma and tumor formation.

The treatment of choice of these tumors owing to their small size is surgical excision. However, they have been removed by various agents, such as caustics, electrocoagulation, and x-ray.

CASE 2.—No. A1692. G. B., an Italian, 28 years of age, entered the New Haven Hospital complaining of a sensitiveness and burning sensation of the left thumb and hand. He attributed his difficulty to the intraspinal injection of diphtheria anti-toxin at 12 years of age, following which he developed pain in the left thumb and

hand with a slight discoloration of the nail. The pain and hypersensitivity had slowly increased since that time. For a number of years he had been able to carry on by avoiding trauma to the thumb. In 1925 he entered the Neurological Institute of New York City where he remained for three weeks. At this time he complained of a burning pain in the left thumb which kept him awake. When he sucked the thumb, the pain shot up the thumb, sometimes skipping the arm, and was felt in the left lower jaw. He also complained of excessive perspiration of the left hand. At times there was a burning of the tip of the little finger and in the second phalanx of the ring finger of the left hand. He described this as if something were forcing its way through his fingers. He stated that his symptoms had been of some years' duration, had progressed slowly, and were worse in winter than in summer. Neurologic examination revealed the skin to be deeply pigmented with several brownish patches such as are found in von Recklinghausen's disease. The deep reflexes were equal and hyperactive, and sensation was normal. The left arm was smaller than the right. The left wrist was like that of a girl's, smaller than the right; and the left hand was the loose, thin, flexible hand of a girl, while the right hand was strong and thick. The left thumb and nail were much smaller than the right. The thenar and hyperthenar eminences were somewhat atrophic on the left. The left thumb nail was thicker and harder than the right. It was noted also that he was of the thin feminine type with the tendencies above noted, and that his voice was high-pitched. Laboratory work was entirely negative; x-ray examination was also negative. It should be noted that the skeleton was x-rayed, except for the left thumb, which was off the film. It was thought that some generalized atrophic disturbance accounted for the slight lack of normal development. The diagnosis was a constitutional ectype and the case was regarded as a pathologic curiosity. In 1928 the patient entered St. Raphael's Hospital, New Haven, where he was operated upon. A rather extensive sympathectomy of the brachial artery was performed. There was no improvement whatever after the operation.

The symptoms continued to grow worse and on April 25, 1934, he entered the New Haven Hospital where the following additional history was obtained. For the past ten years the thumb had become increasingly sensitive. There seemed to be two types of pain, one of which was of the steady, burning character and frequently would awaken him at night, and for which he obtained relief by placing his hand in ice water. The other was a more severe, stabbing type of pain as the result of a blow or when clipping the nail. For years he had cut his nail only with a very sharp razor blade. The pain was worse with a change in weather; also, severe exercise, such as running, would increase the pain. He had noticed that his left hand was always hot and whenever the pain was severe there would be very profuse perspiration. At times the pain would radiate throughout the entire arm, involving the shoulder and side of the face.

Physical examination was essentially negative except for the condition of the arm. The entire arm and hand were smaller than the right. Measurements were as follows:

	RIGHT	LEFT
Biceps	26 cm.	23 cm.
Forearm	25 cm.	22 cm.
Wrist	17 cm.	15 cm.
Hand	21 cm.	17 cm.

The blood pressure of the left arm remained consistently 10 to 15 mm. above that of the right. There seemed to be no demonstrable weakness of any particular muscle group although the entire thumb and hand were somewhat weaker than the right. The skin of the palm of the hand was constantly moist and seemed to be definitely

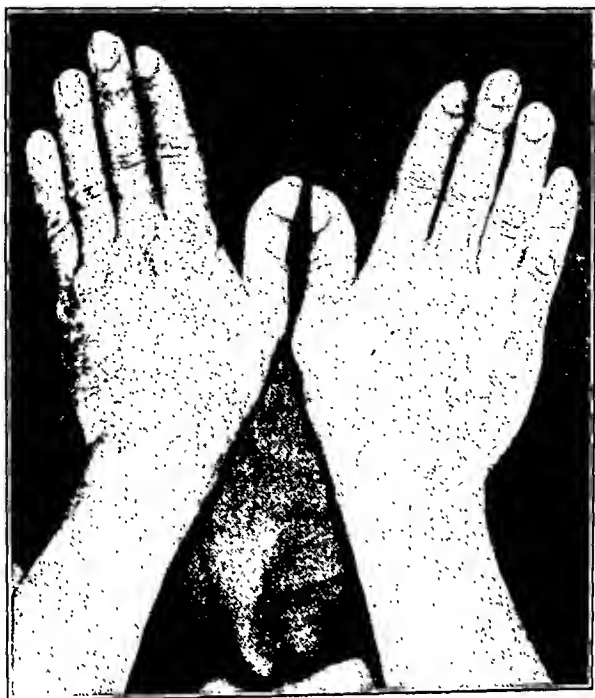


Fig. 7.—Showing atrophy of entire hand as well as thumb.

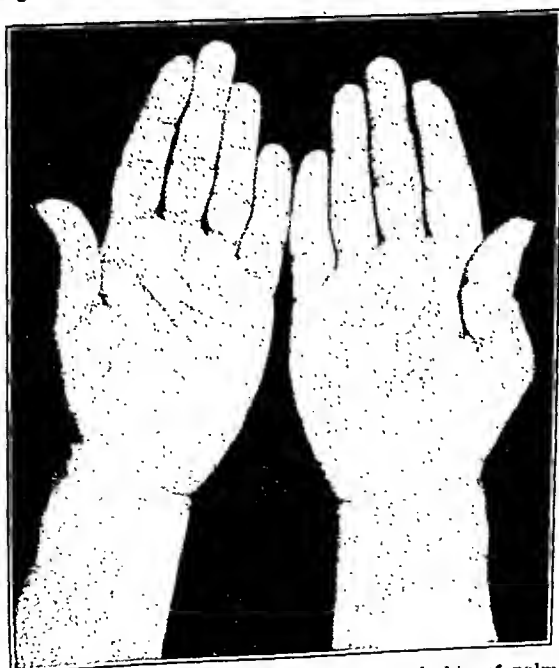


Fig. 8.—Showing atrophy and thin wrinkled skin of palm.

thinner than on the right and was profusely wrinkled. The anterior surfaces of all of the fingers were more sensitive than those on the right. The thumb was exquisitely sensitive over the distal phalanx and the slightest tap with the head of a pin over the palmar surface or over the base of the nail of the left thumb was excruciating. The patient fainted on accidentally striking the thumb. The left thumb was somewhat narrower than the right and showed increased longitudinal ridges. There was a faint bluish discoloration over the base of the nail. Temperature studies showed that the left hand was at a full vasodilation level with the temperature at  $96^{\circ}$  with a room temperature of  $68^{\circ}$  over a period of several hours.

A novocain block of the dorsal sympathectomy was performed on the left. Inasmuch as the hand was at a full vasodilation level, no information could be obtained from this source. However, as the hand was continually sweating and following any painful stimulus to the thumb there was a steady drip from the finger

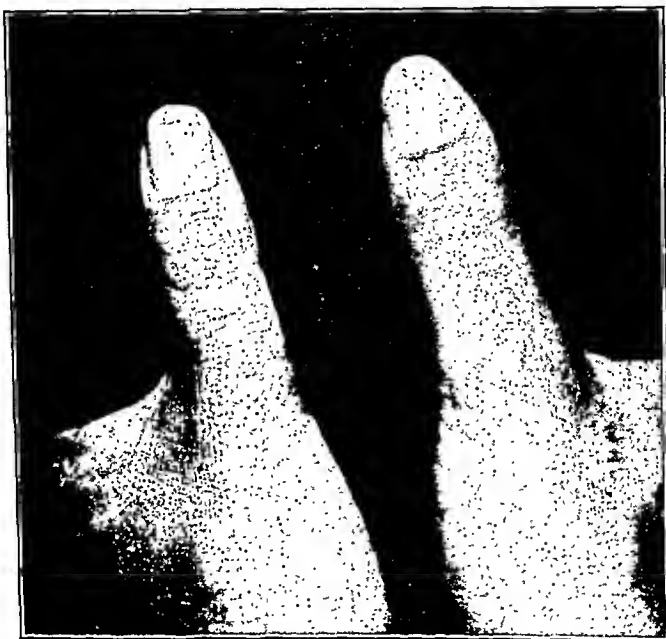


Fig. 9.—Showing atrophy of thumb and longitudinal striation of nail.

tips, this afforded a very good means of determining the effectiveness of the novocain block. Within ten minutes after injection of the novocain, the hand was completely dry, the burning pain and hyperesthesia disappeared, and pain could be elicited only on pressure over the thumbnail.

Roentgenographic examination of the left hand revealed a generalized decrease in the size of all of the bones of the left hand and that portion of the radius and ulna visualized. The osseous structure of all the bones was normal except for the thumb which revealed irregular cystic areas of varying sizes with a coarsening of some of the trabeculae and also an indistinct outline of trabecular markings on the superior and lateral aspect suggestive of destruction. The pathology was confined chiefly to the top and distal portion of the shaft of the terminal phalanx where there was complete destruction of a small area. Roentgenographic impression: primary bone tumor of the terminal phalanx of the left thumb with areas of cystic degeneration.

Oscillometric readings of the left upper arm were only slightly greater than on the right; however, oscillometric readings of the left forearm were nearly twice those of the right.

At operation on May 9, 1934, the nail was incised across the base and removed. Showing through the subungual epithelium was a small, bluish, discolored area. The subungual epithelium was incised longitudinally over the tumor and a flap reflected. This gave a good exposure of the tumor which was extremely vascular. The tumor was readily removed by blunt dissection and although it had scalloped out the terminal phalanx in no place was it adherent. The tumor measured 5 by 4 by 3 mm. A large artery was found to enter the tumor on its anterior surface. Pathologic examination revealed the classical histology as described by Masson.

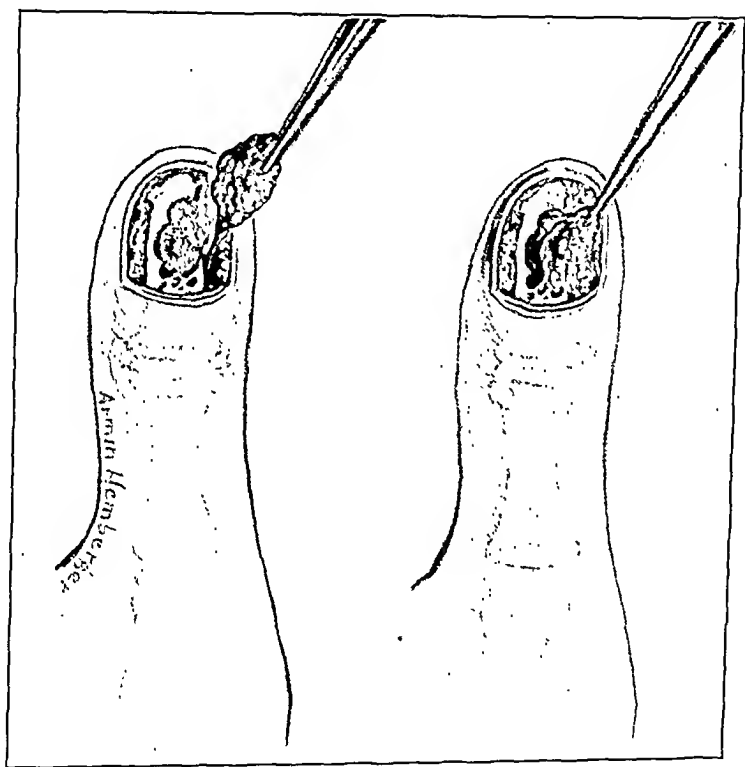


Fig. 10.—Sketch of tumor as seen at operation showing erosion of bone.

**Postoperative Course:** Although four years have elapsed, during which time the patient has been free from symptoms, there has been only slight improvement in the atrophic appearance of the skin and musculature of this hand. In spite of efforts at reeducation the patient does not use his hand with as much freedom as he normally should. It is possible that part of the failure to overcome the atrophic defect may be due to disuse. There is still a slight tendency for this hand to perspire more freely than the normal side.

This case illustrates the extreme radiation of the pain and the profound atrophic developmental changes in muscle, bone, and skin. The relief during the novocain block suggests that the burning, throbbing

type of pain is carried over the sympathetic nervous system, while the failure to obtain relief following the brachial periarterial sympathectomy demonstrates that these fibers leave the artery below this point.

#### IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA (KAPOSI'S DISEASE)

Idiopathic multiple hemorrhagic sarcoma is a rare condition, which, however, is not uncommon in the larger centers with a cosmopolitan population. Dorffels in 1932 found 356 cases in the literature, but this is hardly representative of the incidence since cases are no longer reported unless they present unusual features. A study of the age distribution in this series shows the highest incidence in the sixth and seventh decades. The disease occurs predominantly in males with a ratio of 15 males to 1 female in Dorffels' series. The disease is especially prevalent in men of Italian and Galician birth (MacKee), but, as Dorffel points out, it appears to have a geographic rather than a racial distribution, since the vast majority of cases originate in Russia, Poland, and Northern Italy. Cases, however, have been reported from practically every civilized nation in the world. Another striking feature is the great prevalence of the disease among the laboring classes.

*Clinical Manifestations.*—The disease has a tendency to develop first on the extremities as a unilateral lesion, but during its course it usually becomes bilateral and frequently symmetrical. The disease may be generalized, involving the viscera as well as the cutaneous tissue, but as a rule the first lesions are cutaneous. The eruption is a progressive one which may develop slowly over a period of years with lesions undergoing spontaneous regression, leaving atrophic pigmented scars. The lesions are usually superficial, localized in the skin. The typical lesion is characterized by nodules and plaques of a blue, blue-red, or red-brown color. The lesions vary from 0.2 to 1 or 2 cm. in diameter and are usually multiple. As the disease progresses, coalescence of a number of lesions may result. This may become so extensive that swelling of the extremities approaching an elephantiasis may develop. There is little tendency for ulceration although fungous infection of the overlying hyperkeratotic dermis may occur.

Other lesions which simulate vesicles or lymphangiomas have been described, as well as rapidly growing angiomatous lesions which resemble simple angiomas or granulomapyogenium. The skin lesions as a rule give rise to few subjective symptoms, although itching of the skin is the most common complaint. Occasionally the lesions have been associated with severe pain.

The disease progresses slowly with periods of intermission. The average duration of life is between five and ten years. Death is usually due to intercurrent infection or some complication resulting from extensive visceral involvement.



Oscillometric readings of the left upper arm were only slightly greater than on the right; however, oscillometric readings of the left forearm were nearly twice those of the right.

At operation on May 9, 1934, the nail was incised across the base and removed. Showing through the subungual epithelium was a small, bluish, discolored area. The subungual epithelium was incised longitudinally over the tumor and a flap reflected. This gave a good exposure of the tumor which was extremely vascular. The tumor was readily removed by blunt dissection and although it had scalloped out the terminal phalanx in no place was it adherent. The tumor measured 5 by 4 by 3 mm. A large artery was found to enter the tumor on its anterior surface. Pathologic examination revealed the classical histology as described by Masson.

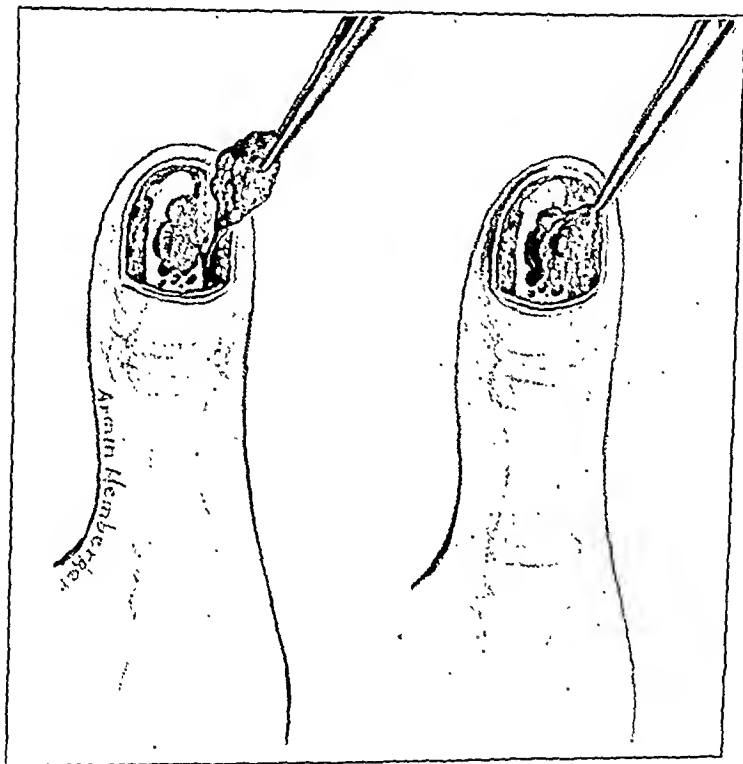


Fig. 10.—Sketch of tumor as seen at operation showing erosion of bone.

**Postoperative Course:** Although four years have elapsed, during which time the patient has been free from symptoms, there has been only slight improvement in the atrophic appearance of the skin and musculature of this hand. In spite of efforts at reeducation the patient does not use his hand with as much freedom as he normally should. It is possible that part of the failure to overcome the atrophic defect may be due to disuse. There is still a slight tendency for this hand to perspire more freely than the normal side.

This case illustrates the extreme radiation of the pain and the profound atrophic developmental changes in muscle, bone, and skin. The relief during the novocain block suggests that the burning, throbbing

filtration of mixed cells—round cells, connective tissue cells and some plasma cells; (c) edema, hemorrhage and iron-containing pigment.

“When the *granulomatous element* is accentuated, the predominating features are (a) proliferation of small blood vessels and also lymphatic vessels; (b) proliferation of connective tissue with young nucleated cells predominating and perivascular infiltration of mixed cells; (c) edema, hemorrhage and iron pigment.

“When the *neoplastic features* predominate the picture varies with the element involved (a) when the changes are principally vascular, the picture may be that of an angioma or may resemble granulation tissue or granuloma; (b) when the lymphatics are involved, the picture may suggest lymphangioma or a mixture of angioma and lymphangioma; (c) when the connective tissue proliferation predominates, fibroma, angiofibroma, angiosarcoma or spindle cell sarcoma may be suggested.

“These lesions are confined primarily to the derma. Changes in the epidermis are secondary and are not pathognomonic nor important. The subcutaneous involvement is usually secondary as a result of extension of the process along the blood vessels.”

While these various lesions may be found at different stages of the disease, and some elements of each found in even the more advanced processes, the earliest lesions present predominantly an inflammatory appearance.

A variety of ideas have been expressed as to the pathogenesis of the disease. Pautrier and Diss feel that it is a neurovascular dysgenesis and a pseudosarcoma, on the basis of one case in which they found cellular derivatives of vascular neuromuscular adnexa and Schwann cell elements. Dorfelfel feels that the disease is primarily one of the reticuloendothelial system which may terminate in malignancy, although he is not willing to call it a reticuloendotheliosis. MacKee and Cipollaro, after careful review of their own material as well as published data, feel that some “unknown systemic agent” attacks the vascular apparatus, causing chronic hyperplastic inflammation and granuloma, and that its histogenesis is compatible with and indistinguishable from that of a malignant new growth or neoplasm. Attempts at transmission of the disease by animal inoculation of suspensions of tissues have yielded negative results, although Justus claims to have produced lesions in rabbits and carried them through several generations.

*Differential Diagnosis.*—The clinical diagnosis is readily established by the progress of the disease, although at various stages it may simulate syphilis, sarcoid, mycosis fungoides, leprosy, and lichen planus. The histologic pathology of the disease is so characteristic, if lesions at various stages of development are examined, that a differential diagnosis is

*Histopathology and Pathogenesis.*—While the pathogenesis of the disease is entirely obscure, the histologic characteristics of the disease are well known. MacKee and Cipollaro have described the lesion in detail as follows: "Three pathological processes are recognized (1) inflamma-

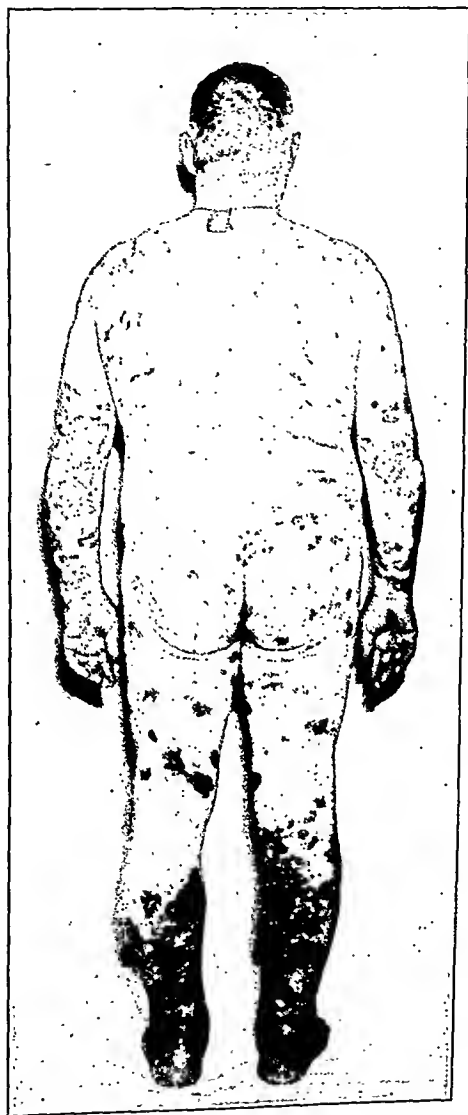


Fig. 11.—Kaposi's disease, showing plaque-like lesions with many coalescent on extremities (note elephantiasis-like swelling of legs).

tory; (2) granulomatous; (3) neoplastic. Very often these processes overlap and produce a borderline or mixed picture.

"When the *inflammatory process* predominates the cardinal features are (a) dilatation of blood vessels and lymphatics; (b) perivascular in-

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easily made. It is important, therefore, to examine several lesions because one alone may be misleading.

*Treatment.*—Most authorities agree that roentgen therapy offers the best results, although recurrence is likely sooner or later. Most of the lesions, as well as symptoms of pain and itching of the skin, disappear promptly with x-ray. MacKee advises repeated small doses of about 75 r. administered once a week to the area of involvement. These may be continued for ten to fifteen weeks. If the lesions are small, larger doses may be used. Small lesions respond equally well to radium. Arsenic administered by mouth, either as Fowler's solution or Asiatic pills, or subcutaneously, intramuscularly, or intravenously, has been used, but it is considered of questionable value at the present time. Small lesions can be cured by surgical removal. Several cases of disappearance of the lesions following treatment have been reported, although it must be emphasized that the disease is a slowly progressive one and that the follow-up on none of these cases has been sufficiently long to consider them cures.

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## TUMORS OF THE SYNOVIA, TENDONS, AND JOINT CAPSULES OF THE HANDS AND FEET

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A LARGE portion of the soft tissues of the hands and feet consists of tendons, their synovial sheaths, and the joint capsular tissues. A variety of both benign and malignant tumors arises from them, but, with the exception of the so-called ganglion, such neoplasms are not common. In general, the benign tumors appear quite circumscribed, and, when not very large, their close association with a tendon, sheath, or joint capsule is readily surmised upon clinical examination. A history of slow growth and variability of pain and tenderness are characteristic of benign processes. Benign tumors may interfere with function when so situated, or when they attain large enough size to prevent the free gliding of tendons through their sheaths or beneath annular ligaments, or when there is mechanical obstruction to full range of motion of a joint. On the other hand, they may extend about the sheaths and tendons, producing large soft masses without causing functional impairment.

Differential diagnosis from acute infectious processes in the tendon sheaths usually is not difficult. In the latter there is, of course, rapid onset, fever, severe pain, sometimes superficial evidence of acute cellulitis, and often a history of a recent wound. Differentiation from chronic inflammation may be more difficult in some cases. In such inflammations an entire sheath is involved; whereas, in the case of a neoplasm the process is usually well circumscribed. Inflammatory thickenings tend to be soft and "fleshy"; whereas, most tumors, except for lipomas, are more firm. Diffuse chronic inflammatory changes in the synovia of the hands and feet sometimes may be a localized manifestation of a generalized arthritis. In differentiation from tuberculous synovitis the following points favor the latter: (1) Sensory or functional symptoms may precede the development of swelling (Mason<sup>1</sup>); (2) the soft swelling may be of sudden onset and may progressively follow the course of the sheath; it usually is first apparent at the wrist; (3) rice bodies (osteochondromatosis may give rise to a similar palpable sign); (4) greater functional disturbance than usually caused by tumors.

Roentgenographic examination of the hand and foot is also of value in the differential clinical diagnosis. The soft tissue shadows cast by such neoplasms serve to indicate to some extent their deeper exten-

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cystic spaces. Aspiration of the viscid fluid with reinjection of a drop or two of iodine, phenol in glycerin, or sodium morrhuate followed by a compression bandage is another form of conservative management.

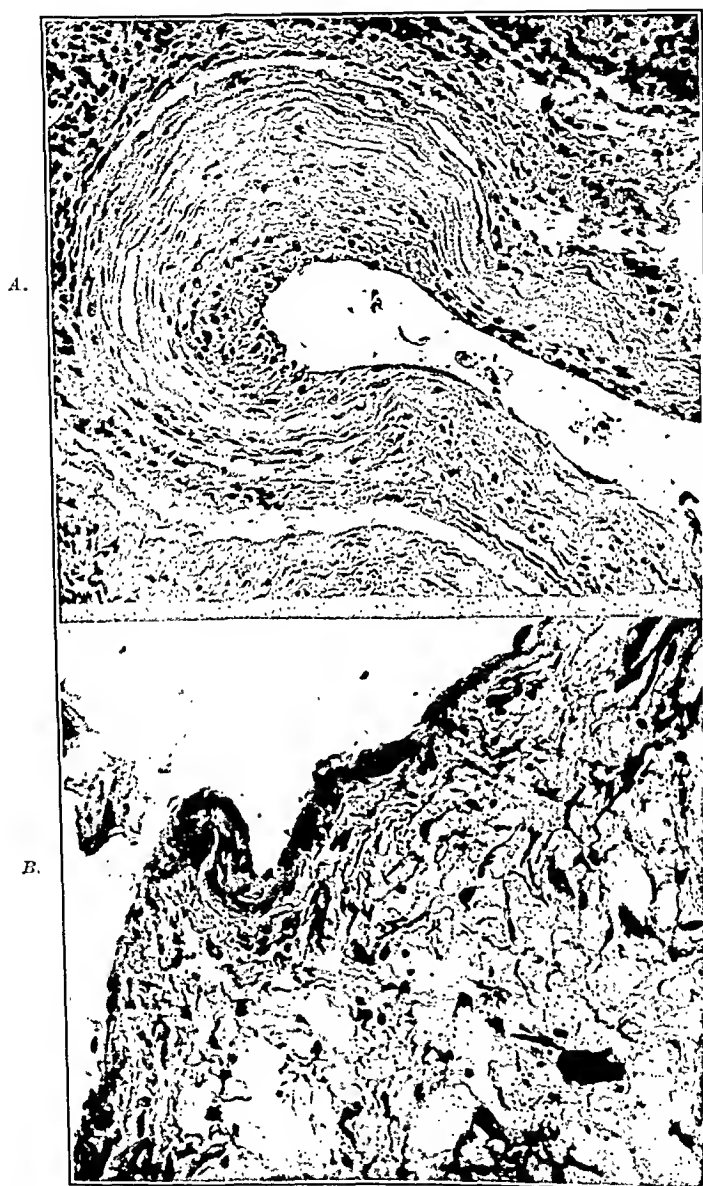


Fig. 2.—Showing various histologic appearances of the walls of ganglia of tendon sheaths and joints. A, Photomicrograph ( $\times 200$ ) of dense fibrous wall, mature cells, and some "pavement" cells lining the cavity; B, photomicrograph ( $\times 250$ ), showing definite lining of cavity and myxomatous-like tissue in the wall.

Bearse<sup>3</sup> recently has stated that the aspiration treatment is more effective if a large gauge needle is employed to permit thorough drainage of the fluid contents.



sions. Because of the marked difference in absorption of rays by fat, as compared to the other tissues, it should be possible to make a roentgenographic diagnosis of lipoma when this is not certain from clinical inspection. Secondary involvement of bone, such as obtains in certain cases of xanthomas arising near the insertion of tendons or in joint capsules, also may be demonstrated. Osteochondroma and osteoma of the tendons and sheaths afford characteristic shadows but must be differentiated from sesamoid bones.

*Ganglion.*—This is a common condition of the hands and feet, observed most often on the dorsal aspects of the wrist (Fig. 1). Other frequent sites are the dorsal aspect of the ankle, foot, and palmar surface of the wrist. They may also arise from tendon sheaths and in rare instances in tendons themselves. They form firm smooth rounded



Fig. 1.—Oval and flattened cystic mass on the dorsum of the wrist. At operation this proved to be a ganglion arising from the underlying extensor tendon sheaths.

masses which upon palpation yield the sensation of fluid under pressure. It is generally held that these lesions are not herniations of the synovia but the result of fibroplasia in which isolated areas of colloid degeneration appear, which in turn coalesce to form a large uni- or multiloculated cyst filled with clear viscous fluid.<sup>2</sup> Microscopic examination of the wall reveals it to be composed of dense fibrous tissue and the lining of the larger cystic spaces sometimes resembles synovia with an occasional villus (Fig. 2A). Foci of myxomatous changes may be present in the wall, especially the base (Fig. 2B).

That trauma may be an etiologic factor is suggested by the fact that ganglions are often observed in persons who use their hands a great deal, such as typists, musicians, etc.

Conservative treatment consists in striking the mass with a hard flat surface, such as a book or board, in order to collapse the principal

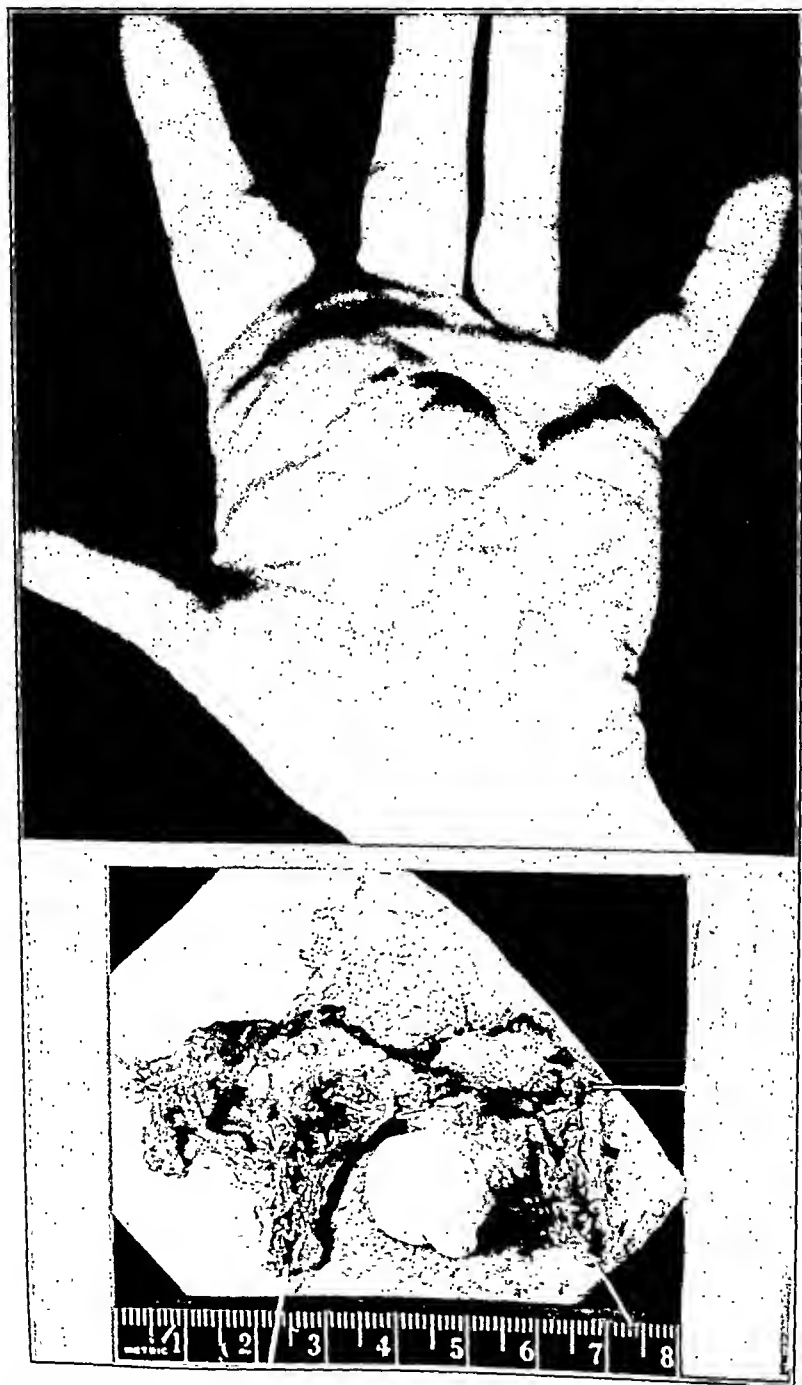


Fig. 3.—A, Fleshy tumor of palm of hand and base of index finger, present since childhood, and a localized manifestation of generalized von Recklinghausen neurofibromatosis. There was no functional impairment. B, Photograph of excised specimen showing plexiform neurofibroma with one definite myxomatous portion (the white mass attached to lower margin).

The treatment of choice is generally conceded to be excision. A transverse or longitudinal incision is made over the mass and the latter excised in toto if possible. Where there is a broad attachment at the base, the ganglion is usually punctured during the operation. Closure of the wound is performed without drainage. Recurrences are not rare due to incomplete excision, especially of the base.

Large complex, multiloculated *ganglia* with rather extensive development about sheaths and tendons have been described. Compression of fluid from one portion to the other is a characteristic sign. The treatment is excision, which may necessitate large incision and careful extensive dissection to free the structure in toto.

*Fibroma*.—These lesions are rare in close association with the tendons, sheaths, and joint capsular tissues of the hands and feet.<sup>4</sup> They form small, firm, well-circumscribed nodules which may or may not be tender. Their true nature cannot be finally determined until examined microscopically since clinically they are not distinguishable from other tumors of these structures.

In some instances "snapping" digits are the result of small rounded or fusiform dense fibrous masses in the tendons, and, when at operation the area is exposed, these growths may be shelled or cut out of the tendon and the latter thus reduced in size to permit normal function.<sup>5</sup>

Multiple or single superficial or deep fibromas may be observed in the hands and feet as part of a generalized neurofibromatosis of von Recklinghausen. I have observed two such cases in adults, in one of which a large fleshy mass was removed from the deep palmar space for cosmetic purposes, the growth having been present since childhood (Fig. 3).

*Xanthoma or Giant Cell Tumor of the Tendons and Sheaths*.—The question of whether these processes represent true neoplasms or are a local manifestation of some obscure disturbance in fat metabolism has not yet been settled.<sup>6</sup> They are observed in patients of all ages, and usually grow slowly. Pain or tenderness is absent or not a prominent symptom. They occur more often in the hands than the feet. They form moderately soft or firm rounded, coarsely nodular masses in the digits near tendinous insertions (Fig. 4), from which points they arise or they may be firmly attached to the wrist or ankle joint capsules, or they may develop extensively about the flexor or extensor tendons arising primarily in the sheaths. Secondary invasion of bone with limited destruction of the latter has been observed in some cases where these neoplasms arise from tendinous insertions or bony attachments of joint capsules. In some cases xanthelasmas of the skin in other parts of the body<sup>7</sup> and hypercholesteremia may be associated with these tumors.

The gross appearance is mottled yellow, yellow-brown, and gray, and this is quite characteristic. Histologic examination (Fig. 5) re-

veals a groundwork of dense fibrous tissue in which are scattered spindle and rounded cells, foreign body giant cells, sparsely distributed or in large numbers, and aggregates of large lipoid containing foam cells, macrophages with brown pigment, and sometimes cholesterol crystals. In a few instances the stroma contains islands of cartilage and even a few bony trabeculae.

*Treatment:* Excision is advised because of cosmetic, functional, or other reasons, and, as soon as the masses are exposed through limited incisions over them, their true nature is apparent because of their color. When not large they tend to bulge through the incisions of access and may be easily removed. A small pedicle of attachment to sheath or tendinous insertion is often found and in the latter attachment secondary invasion of bone may be present. This is removed by curettage. Extensive spread about the tendons may require large incisions and careful and prolonged dissection for removal. Recurrences are rare but occur presumably from fragments of the process left behind.

*Prognosis:* Since the tumors are benign, the prognosis is good.

*Lipoma.*—While the larger joints such as the knee, shoulder and hip, are the common sites of synovial lipomas, they also, in rare instances, occur in the association with the sheaths of the hands and feet, forming soft or moderately firm compressible masses which have slowly increased in size. Of 34 cases in the hands reviewed in the literature by Straus,<sup>8</sup> only 1 was recognized as such before operation (Filho). They develop as lipomatous or fibrolipomatous bodies within the tendon sheath or about it. In the hands they may be confined to the fingers, extend for some distance along the tendons, or be confined to the level of the mid-palmar space. They may be symmetrical in both hands. In Straus' case of lipoma of the flexor sheath of the fourth finger arising at its palmar terminus, the mass extended backward under the palmar fascia into the interdigital spaces on either side of the fourth finger and in dorsal direction along the lumbrical tendons on either side of the finger to produce a bulge on the dorsal aspect of it. Excess pads of fat developing about the malleoli in one or both ankles are sometimes considered to be lipomas. Gosselin suggested that lipomas change from a soft to a more firm consistency when their temperature is substantially lowered by application of an ice bag. Straus confirmed the clinical value of this test.

Grandelaude, Razemon, and Bizard<sup>9</sup> reported a spectacular case of arborescent angioliipoma of the flexor pollicis longus tendon, which, after its presence had been noted for several months by the patient, apparently produced a spontaneous rupture of the tendon.

*Treatment:* Excision of lipomas of the tendon sheaths is performed often through limited incision because when overlying pressure is re-



Fig. 4.—Coarsely nodular tumor on palmar aspect of ring finger of left hand, two years' duration, in 44-year-old white female. At operation, through small linear incision along outer margin of palmar aspect of the swelling, a brownish soft mass was easily shelled out and found to arise from the flexor tendon sheath. Microscopic examination: xanthoma.

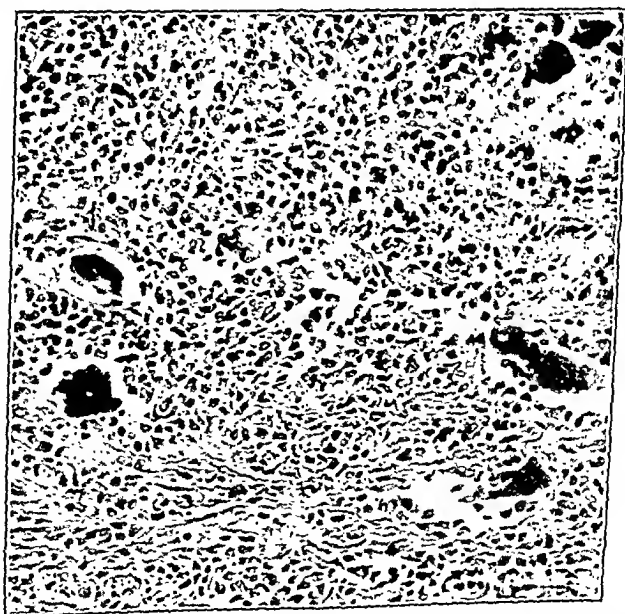


Fig. 5.—Photomicrograph ( $\times 270$ ) of portion of xanthoma or giant cell tumor of tendon sheath shown in Fig. 3. Note foreign body giant cells and stroma of rounded and spindle cells.

the synovial membranes themselves and reproduce very distorted histologic pictures reminiscent of synovia. There is a groundwork of rounded or spindle cells with varying amounts of collagen. Scattered

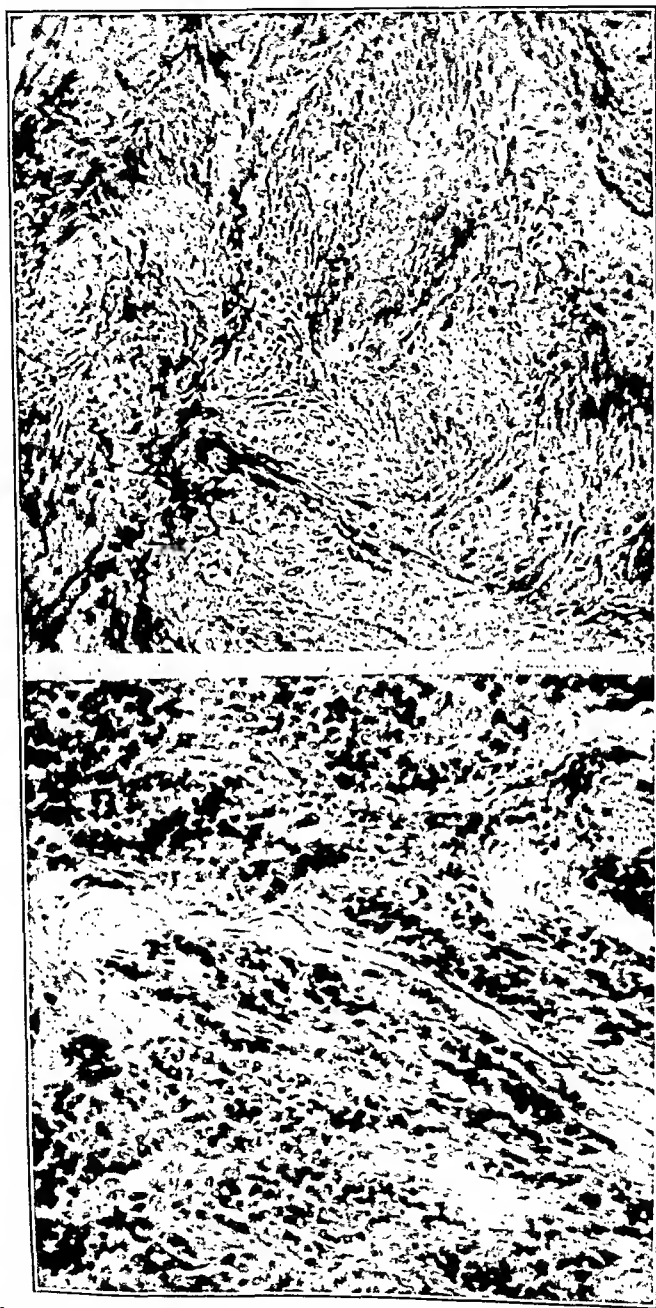


Fig. 6.—Photomicrograph ( $\times 270$ ) of A, synovioma arising in tendon sheaths below internal malleolus of ankle in 36-year-old male. Note irregular cords of epithelial-like cells alternating with bundles of thin spindle cells. B, Round cell sarcoma of plantar fascia in 39-year-old female. Excision was followed by widespread subcutaneous metastases and death in six months.

lieved they tend to bulge into the field. On the other hand, minute ramifications may necessitate extensive and meticulous dissection to avoid injury to nerves, tendons, and vessels. Regardless of size or complex structure, lipomas of the tendon sheaths usually have rather limited pedicles of attachment. It is important to identify and completely excise these pedicles as well as all portions of the tumor because incomplete excision may in time be followed by recurrences.

*Osteochondroma and Osteoma.*—These growths are among the rarer ones observed in the tendons, sheaths, and joint capsules of the hands<sup>10</sup> and feet,<sup>11, 12</sup> but are not so very rare in the larger joints, such as the knee, hip, elbow, and shoulder. While in the latter locations they are usually multiple in the joint synovia and sometimes regarded as metaplasia on an inflammatory basis, those few observed in the hands and feet are considered to be true neoplasms.

While often referred to as situated in the tendons, in most instances described in the literature operation revealed a primary pedicle of attachment to the sheath frequently near the osseous insertion of the tendon. Tenderness and some swelling may be present, especially following exercise of the part, and there may be serious functional impairment. On clinical examination a small firm mass may be palpated. If composed principally of cartilage it may be sufficiently elastic to afford an impression of ganglion, as occurred in the case cited by Chauvain and Roux.<sup>13</sup>

Histologically the growths resemble benign chondroma with areas of calcification and ossification. Malignant degeneration to formation of chondrosarcoma has been observed (see below).

The treatment is excision.

#### MALIGNANT TUMORS

Malignant tumors of the tendons and sheaths in the hands and feet are quite rare. The clinical history is usually that of a firm swelling which may exhibit rapid or at first slow growth and which is often excised locally only to recur at the old site or in the surrounding tissues. Pain and tenderness vary both as to severity and time of onset, coming sometimes after the lesion has become well established. Because the hands and feet are so exposed to trauma, it has not been difficult to obtain clinical histories showing that the process began, at least in the patient's opinion, as the result of a single severe or of repeated traumatizations. In this group may also be placed the firm dense, often bulky, infiltrating sarcomas which arise from the plantar or palmar fascias.

Histologically, there are four types of neoplasms in this category: (1) Synovioma (Fig. 6A). These tumors have been described in the earlier literature under a variety of names<sup>14</sup> because of their peculiar histologic appearance. They are generally regarded as arising from

and when roentgenograms of the chest show no evidence of pulmonary metastases.

*Irradiation Therapy:* Experience to date has indicated that these neoplasms are radioresistant and therefore little is to be expected from such treatment, although it is indicated where surgical procedures are refused.

*Prognosis:* The prognosis in general is poor, yet some cases have survived for long periods and others after surviving long periods have died of pulmonary metastases. Coley and Pierson<sup>15</sup> recently have published an excellent summary of the question of synovioma, reviewing the literature and the series of the Memorial Hospital.

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throughout are cords or tubules of cuboidal or low columnar epithelium-like cells. In some cases small papillary cystic structures are formed where the infolded papillomatous process is not a great deal unlike a synovial villus. Mitoses in the different cells vary and their frequency in this type of tumor is no indication of malignancy. (2) So-called spindle cell sarcoma.<sup>12</sup> These tumors appear to be quite uncommon, arising from the tendons, sheaths, or joint capsule in the hands and feet, and indeed it may not be possible to ascertain the exact point of origin in cases that are first seen presenting a dense infiltrating mass. They may be composed of uniformly small cells, large spindle cells, or both types. The question of a neurogenic origin to such tumors has been discussed by Ewing and Stewart. (3) Round cell sarcomas (Fig. 6B). Tumors composed of small round cells with scanty cytoplasm and producing no stroma develop in the soft parts of the body and have been observed as primary in the hands and feet. I have had occasion to see such a patient who presented a dense egg-sized mass in the sole of the foot and who a few weeks later exhibited fulminating metastases in the subcutaneous tissues over the body and in the lungs. (4) Malignant degeneration of osteoarthritic tendinous or synovial tumors or primary malignant chondrosarcomas of these structures have also been described.<sup>4, 12</sup>

*General Remarks Concerning the Treatment of Malignant Tumors.—*

In general the treatment of choice for sarcomas well out upon an extremity is amputation at a level consistent with the principle of wide resection. In the case of the wrist or hand this should be in the mid-forearm, and for the ankle or foot, through the junction of the upper third with the lower two-thirds of the leg. Such treatment is indicated for primary sarcomas in the hand and foot, where the diagnosis is confirmed by biopsy and where there is no clinical evidence of axillary or inguinal lymph node or pulmonary metastases.

The question is not easily solved, however, in many of these cases where the lesion when first examined appears as a rather small, well-delimited process, and where excision, not very radical, was performed under the impression that the growth was not malignant. Microscopic study which should be done upon all such growths, when it reveals a malignant tumor, leads to a reconsideration of the future management. Where the appearance is that of a rapidly growing process, amputation should be advised. Where a synovioma is described that does not appear to be rapidly growing, and excision has been grossly wide of the lesion, postoperative x-ray therapy with frequent observation of the patient may be followed. Where it is feasible to reoperate and excise the tumor site more widely, this should be advised. The subsequent development of subcutaneous firm nodules in and about the excised tumor site should constitute an indication for amputation when biopsy of a nodule reveals its sarcomatous nature

The treatment rendered and the results obtained are given in Table I, and will be discussed under the different types of tumors.

From the American and foreign literature we were able to collect a total of 609 cases of tumors involving the bones of the hands and feet. These are summarized in Table III. Some of these cases are individually reported and again included in another author's series, so that there may be some duplication. However, we have attempted to recognize this possibility and to report each case but once. Again, considerable difficulty is experienced because of inadequate details in the original report. Diagnoses are often inconclusive; the location is frequently inadequately described; scant details of the treatment are given, and in only a few instances are adequate follow-up reports available. Under these circumstances, we have endeavored to compile the statistics as given in our table as accurately as possible, with careful reference to the original report. The total number is greatly augmented by many instances (205) of subcalcaneal exostoses. There is a remarkable sparsity in the literature of all other types of primary bone tumors of the hands and feet. The proportionate number roughly corresponds to our series. The number of cases for each bone involved is shown under the various diagnoses in Table III.

*Osteogenic Sarcoma.*—There were 12 cases of osteogenic sarcoma in our series and 37 in the literature. The symptoms noted were those found in osteogenic sarcoma in general; i.e., pain in the region involved followed shortly after by swelling and disability. There is a hard, palpable swelling which increases in size with relative rapidity. The roentgenographs show characteristic irregular bone destruction with laying down of new bone (Fig. 1), often with a sun-burst appearance. Aspiration biopsy as recommended by Coley, Sharp, and Ellis, is a valuable aid in the accurate diagnosis of this tumor and should be done to verify the clinical and roentgenographic findings. Many of these tumors are secondary to a benign chondroma and represent a malignant transformation of a simple chondroma to an osteochondrosarcoma (Fig. 2). Not infrequently trauma is the alleged cause of this transformation. In other cases the tumors are of the fibrosarcoma variety, and these in our opinion offer a more hopeful prognosis. Five of our patients are alive and well (3 for more than five years); 4 died of pulmonary metastases from one to three years after admission; and 1 died following a prostatectomy nine years after amputation of the foot for osteogenic sarcoma. The other 2 have been lost to follow-up, but 1 is undoubtedly dead, as he had pulmonary metastases six months after treatment. From our five-year survival rate (33 per cent), it would appear that osteogenic sarcoma of the bones of the hands and feet offers a more favorable prognosis than does the same condition in other bones. It is our opinion that once a diagnosis of osteogenic sarcoma has been

## TUMORS PRIMARY IN THE BONES OF THE HANDS AND FEET

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IT IS ONLY very rarely that tumors of any type originate in the bones of the hands and feet. Statistics of the Memorial Hospital as well as an extensive review of the literature substantiate this statement. As has been pointed out by Kahn, malignant tumors of these bones are exceedingly rare. Schreiner and Wehr surveyed a series of 10,459 cases of malignant disease over a nineteen-year period and could find only 37 involving the foot, and only 4 of these were bone sarcomas. Of 1,740 bone tumors at Johns Hopkins Hospital, Moore found 46 benign and malignant tumors of the foot. Considering the fact that there are 206 bones in the entire skeleton, 106 of which are in the hands and feet, the disproportion in their relative frequency of involvement is apparent.

In a total of 1,211 bone tumors at Memorial Hospital and the Hospital for Ruptured and Crippled, we have found only 47 instances of involvement of the bones of the hands and feet. These are shown individually in Table I and summarized in Table II.

Sex, apparently, is an unimportant factor. In the series of 47 cases mentioned, 23 were males and 24 were females.

Regarding age, the youngest patient was 5 years of age, and the oldest, 65; the average age was 28.3 years. There were 7 cases in the first decade, 10 in the second, 12 in the third, 9 in the fourth, 4 in the fifth, 2 in the sixth, and 3 in the seventh. Thus the majority of patients (31) were between 10 and 40 years of age.

Twenty tumors involved the bones of the hand and 27 the bones of the foot. Six occupied the metacarpal bones, and 14 the phalanges of the hand (10 in the proximal, 2 in the middle, and 2 in the distal phalanges). One tumor occurred in the astragalus; 10 in the calcaneus, and 1 in the cuneiform. Ten were found in the metatarsals and 5 in the phalanges of the foot (none in the proximal, 3 in the middle, and 2 in the distal phalanges).

There were 12 cases of osteogenic sarcoma, 6 of Ewing's endothelioma, and 9 giant cell tumors. Exostoses and chondromyxomas are included under the heading of chondromas, of which there were 15. There were 2 simple cysts, 2 metastatic lesions involving the bones of the hands and feet, and 1 angiosarcoma.

TABLE I—CONT'D

	S. H.	M		Giant cell		4/28/24	X-ray		2/ 3/25	Final	Not traced
23	J. H.	M	17	L. metacarpal, iii	Metastatic	3/18/28	Radium		4/20/28	Died	Primary hypernephroma
24	J. H.	M	40	R. astragalus	Endothelioma	10/25/24	Excision	radium, x-ray	4/30/25	Died	
25	E. K.	F	23	L. metatarsal, i	Chondroma	12/11/36	Excision		4/ 6/38	Well	Pyogenic granuloma
26	G. K.	F	13	L. phalanx, P, hand	Osteochondroma	12/ 1/36	Excision		4/18/38	Well	
27	B. L.	M	13	L. phalanx, D, foot	Osteochondroma	2/25/35	Excision		3/22/37	Well	
28	M. M.	M	35	R. phalanx, M, hand	Osteochondroma	9/20/34	X-ray		1/20/37	Final	Not traced further
29	A. M.	F	53	L. calcaneus	Giant cell	7/22/26	Curettage		11/15/37	Well	
30	H. N.	M	32	R. metatarsal, i	Giant cell	3/18/20	Radium		5/15/23	Final	Not traced further
31	S. P.	F	65	R. metacarpal, iv	Chondroma	1/20/31	Curettage		-	-	No follow-up
32	H. P.	F	8	L. phalanx, P, hand	Cyst	9/21/31	X-ray		11/ 9/36	Well	
33	E. R.	M	29	R. phalanx, P, hand	Chondroma	5/19/33	Amputation		5/16/35	Died	Pulmonary metastasis
34	M. R.	F	34	L. metatarsal, ii	Osteogenic	12/14/35	None		-	-	No follow-up
35	R. S.	F	63	R. phalanx, P, hand	Chondroma	9/ 3/24	Excision, radium, x-ray		6/ 9/27	Final	Pulmonary metastasis
36	P. S.	M	19	R. metacarpal, i	Osteogenic						1/30/25
37	T. S.	M	27	L. calcaneus	Endothelioma	4/ 2/22	X-ray		6/30/24	Final	Not traced further
38	J. S.	M	65	R. metatarsal, v	Osteogenic	5/ 8/31	X-ray, amputation		11/17/37	Well	
39	R. S.	F	16	R. phalanx, D, foot	Osteochondroma	6/ 6/34	Excision		7/21/37	Well	Pyogenic granuloma
40	C. S.	F	5	L. calcaneus	Endothelioma	12/ 1/23	Radium		2/15/27	Died	Multiple metastases
41	H. S.	F	17	L. metatarsal, iv	Giant cell	8/30/37	Curettage (recurred), excision		4/13/38	Well	
42	M. S.	F	14	L. calcaneus	Giant cell	10/ 2/29	Curettage, x-ray, amputation		4/19/37	Well	
43	B. T.	F	32	R. phalanx, D, hand	Cyst	8/16/29	Curettage		-	-	No follow-up
44	C. T.	M	9	L. calcaneus	Endothelioma	10/ 3/23	Curettage, radium		4/14/24	Died	Multiple metastases
45	V. V.	M	23	R. metatarsal, i	Osteogenic	7/23/24	Excision, x-ray		1/ 7/28	Final	Not traced further
46	R. V.	M	33	R. metatarsal, iii	Angiosarcoma	4/26/25	Amputation		5/ 5/25	Died	Multiple metastases
47	L. W.	F	34	R. metatarsal, iv	Osteogenic	3/ 3/30	X-ray, radium, eurettage, amputation		2/14/38	Well	

TABLE I  
BONE TUMORS OF THE HANDS AND FEET  
SERIES FROM MEMORIAL HOSPITAL AND HOSPITAL FOR RUPTURED AND CRIPPLED

NO.	NAME	SEX	AGE	BONE*	DIAGNOSIS	ADMITTED	TREATMENT	FOLLOWED	STATUS	REMARKS
1	B. A.	F	25	L. calcaneus	Endothelioma	12/ 3/34	Curettage, x-ray, amputation	12/23/37	Well	
2	G. B.	F	8	L. phalanx, D, foot	Osteochondroma	11/ 3/37	Excision	3/23/38	Well	Pyogenic granuloma
3	I. B.	M	11	L. phalanx, D, foot	Osteochondroma	1/31/38	Excision	2/23/38	Well	
4	R. B.	M	60	L. metacarpal, v	Osteogenic	7/28/20	Excision, radium, amputation	12/ 1/29	Died	following prostatectomy
5	D. B.	F	15	L. calcaneus	Osteogenic	8/ 1/32	Amputation	12/ 9/37	Well	
6	J. B.	F	44	L. phalanx, P, hand	Chondroma	1/ 4/37	Curettage, graft	12/ 9/37	Well	
7	W. C.	F	24	L. metacarpal, v	Osteochondroma	5/27/33	Excision, three times	1/12/38	Well	
8	J. C.	F	25	R. metacarpal, i	Giant cell	11/26/34	Curettage, x-ray	12/ 2/36	Final	Not traced further
10	E. C.	M	5	L. calcaneus	Osteogenic	8/21/35	Amputation	10/26/36	Died	
11	E. C.	F	37	L. calcaneus	Giant cell	10/31/34	X-ray	5/ 6/32	Well	
12	F. C.	F	30	R. phalanx, P, hand	Chondroma	9/22/22	Radium	1/ 6/26	Final	Not traced further
13	W. C.	M	30	L. phalanx, P, hand	Osteochondroma	6/28/33	Excision	6/30/37	Well	
14	D. D.	M	33	R. phalanx, P, hand	Osteogenic	2/10/37	Amputation	6/25/38	Well	
15	S. D.	M	33	R. metatarsal	Osteogenic	8/25/29	Amputation	5/11/32	Well	
16	T. E.	M	8	R. phalanx, D, foot	Osteochondroma	3/26/30	Radium	5/14/30	Final	Not traced further
17	L. E.	M	13	L. phalanx, D, hand	Giant cell	12/12/35	Amputation	6/29/38	Well	
18	C. F.	M	30	R. phalanx, P, hand	Chondroma	9/25/36	Curettage	4/13/38	Well	
19	W. F.	M	50	R. metatarsal, iii	Endothelioma	10/17/24	Excision, radium	9/26/26	Died	Multiple metastases
20	A. G.	M	16	R. calcaneus	Osteogenic	3/18/30	Excision, radium	7/14/33	Died	Multiple metastases
21	J. G.	F	26	R. cuneiform	Osteogenic	6/12/24	Amputation	9/ 2/26	Died	Multiple metastases
22	M. G.	F	41	L. phalanx, P, hand	Osteochondroma	4/18/31	None	4/13/32	Final	Not traced
				R. phalanx, D, hand	Metastatic	4/22/34	Amputation	10/29/37	Died	Primary parotid

\*D, distal; P, proximal.



TABLE II

SUMMARY OF MEMORIAL HOSPITAL AND HOSPITAL FOR RUPTURED AND CRIPPLED CASES

	OSTEO- GENIC SAR- COMA	EWING'S ENDOTHE- LIOMA	GIANT CELL TUMOR	CHON- DROMA	CYST	METAS- TATIC	ANGIO- SAR- COMA	TOTAL
Metacarpals	2		2	2				6
Phalanges 1	1		1	7	1			10
Phalanges 2			1	1				2
Phalanges 3					1			2
Astragalus						1		1
Calcaneus	3	4	3			1		10
Tarsals	1							1
Metatarsals	5	2	2				1	10
Phalanges 1				3				3
Phalanges 2				2				2
Phalanges 3								
Total	12	6	9	15	2	2	1	47

made the treatment of choice is primary amputation. Local excisions and resections, with or without irradiation, have been tried by others, but we know of no five-year cure following these procedures. Of course, partial amputations of the hand and foot may be justified according to the extent and location of the lesion (Fig. 3). Thus, it may be possible to preserve a portion of the member and leave the patient with a functionally useful remnant, an impossible accomplishment when dealing with tumors of other parts of the skeleton.

*Endothelioma (Ewing's Sarcoma).*—We have 6 cases of this condition in our series, and there are 31 in the literature. The onset is often indefinite and a diagnosis of chronic osteomyelitis frequently is erroneously made. Again, pain is the earliest symptom and there is often fever. The roentgenograph shows bone destruction of a more

TABLE III

SUMMARY OF CASES COLLECTED FROM THE LITERATURE

UPPER	OSTEOGENIC	ENDOTHELIOMA	GIANT CELL TUMOR	CHONDROMA	MYXOMA	CYST	METASTATIC	EXOSTOSIS	OSTEOID OSTEOOMA	SARCOMA	TOTAL
Carpals	2	1		7	1	1		4			6
Metacarpals	2		11	54	7	16		12	1		29
Phalanges		1	9								101
Total (hand)	4	2	20	61	8	24		16	1		136
LOWER											
Astragalus	3		10	1	1	3			1		19
Calcaneus	21	21	17	4	1	7	1	205	1	1	279
Tarsal (other)	4		5	2		2	2	3		1	19
Metatarsal	3	6	9	7		5	2	3		3	38
Phalanges	2	2	4	16	1	6	2	84	1		118
Total (foot)	33	29	45	30	3	23	7	295	3	5	473
Total	37	31	65	91	11	47	7	311	4	5	609

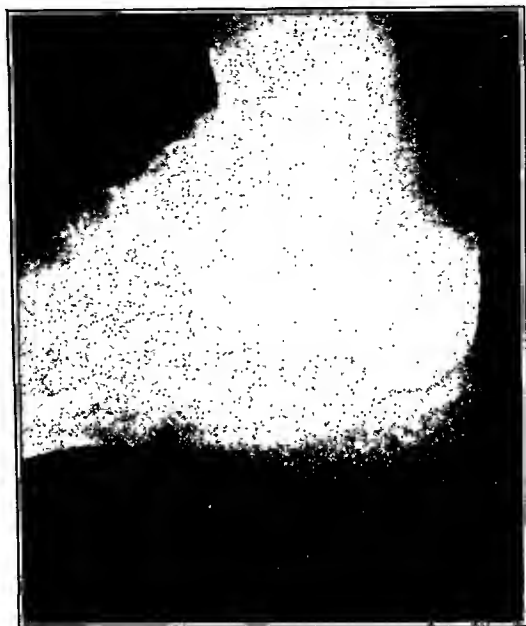


Fig. 1.—Case 5. Osteogenic sarcoma of the os calcis. Female, aged 15 years. Amputation below the knee. Alive and well 5½ years later.



Fig. 2.—Case 38. Osteogenic chondromyxosarcoma of fifth metatarsal. Male, aged 65 years. Diagnosis by aspiration biopsy. Amputation of fourth and fifth metatarsals. Alive and well 7½ years later.



or less diffuse nature, but the fusiform shape and the periosteal splitting (features characteristic of this disease in the long tubular bones) are less frequently demonstrable. In this type of tumor, also, aspiration biopsy is relatively simple and accurate and should be attempted if there is any doubt as to the diagnosis of a destructive bone lesion. The condition is frequently referred to in the older literature as round cell sarcoma, later as endothelial myeloma, and currently as endothelioma or Ewing's sarcoma. Probably some hemangioendotheliomas



Fig. 3.—Case 13. Low grade osteogenic sarcoma of proximal phalanx of fifth finger. Male, aged 30 years. Two operations elsewhere for inflammatory disease. Amputation of fourth and fifth fingers through metacarpals. Alive and well 1½ years later.

and unclassified sarcomas belong in this group. One of our cases was diagnosed following curettage for osteomyelitis of the os calcis; heavy irradiation was given, followed by amputation and a prolonged course of Coley's toxins; the patient is well more than three years after with no evidence of metastasis or recurrence. Four other patients (2 os calcis and 2 metatarsal bone) died of multiple metastases from nine months to three and one-half years after treatment. One case

was lost to follow-up after two years. It is, therefore, fair to assume that the prognosis of this condition is generally poor. However, it is our impression that the treatment of choice, following early diagnosis, is heavy irradiation followed by amputation and a post-operative course of injections of Coley's toxins. Connor reports a patient of Thompson's in the Bone Sarcoma Registry who died following a gall-bladder operation eight years after amputation of the foot for endothelioma of the os calcis.



Fig. 4.—Case 16. Aneurysmal giant cell tumor of distal phalanx of thumb. Male, aged 13 years. Amputation through proximal phalanx. Well two years.

*Giant Cell Tumor.*—In addition to 9 giant cell tumors in our own series, we found 65 reported in the literature. Vague pain is usually an early symptom. Not infrequently, however, slight swelling or pathologic fracture is the first symptom, as these tumors are benign and grow relatively slowly. They may attain considerable size before the patient seeks medical relief (this was true of one case in our series [Fig. 4]). The roentgenographic appearance is usually quite characteristic and shows a round or oval centrally placed lesion with many fine trabeculations, usually well demarcated and with a thinned but intact cortex (Fig. 5). The clinical and roentgenographic features are usually sufficient to make a diagnosis. Aspiration biopsy may be tried if the cortex

is very thin, but it is not as useful in this type of tumor, as they are usually centrally placed. The terms hemorrhagic osteomyelitis and myeloid sarcoma appearing in the literature are synonymous. In the microscopic picture numerous giant cells are characteristic, but the aggressiveness of the tumor depends upon the fibrous tissue stroma which must be given due consideration in the ultimate pathologic diagnosis.

Following a recent extensive survey of giant cell tumors in general,\* we have come to the conclusion that the treatment of this con-



Fig. 5.—Case 41. Giant cell tumor of fourth metatarsal. Female, aged 17 years. Curettage at another hospital. Recurred six months later. Resection of metatarsal. Well four months later.

dition is either surgery or irradiation, but never both. Either procedure alone gives satisfactory results; whereas, a combination is fraught with danger. We believe the same principle applies to giant cell tumors of the hands and feet. Irradiation, if used, should be given in moderate doses. Radical surgery, such as amputation or resection, is indicated only in special instances. One of our cases presented a tremendous growth of the distal phalax of the thumb, and amputation was performed as the treatment of choice (Fig. 4). Astragalectomy and resection of the tarsals, metatarsals (Fig. 5), or metacarpals may

\*Coley, Bradley L., and Higinbotham, Norman L.: Giant Cell Tumor of Bone, J. Bone & Joint Dis. 20: 870-884, 1938.

be necessary in recurrent cases. However, curettage, cauterization with zinc chloride, and primary wound closure is indicated in most cases as the primary treatment.\*

*Cyst.*—Our series contains 2 cases of simple cyst, or solitary osteitis fibrosa cystica; whereas, there are 47 cases reported in the literature. In many of the reported cases, however, the diagnosis was based on clinical and roentgenographic evidence alone, but, were a study of the pathologic material possible, we feel sure that not a few would be transferred to the giant cell tumor or chondroma group. These cysts give very few signs and symptoms and are usually picked up as an incidental finding in roentgenographs taken for other purposes. Pathologic fracture is frequently the first symptom. The roentgenograph shows a small rounded area of bone destruction with well-defined margins, but lacking the trabeculations characteristic of giant cell tumors. Operation usually reveals a thin, fibrous lining of the cyst wall, containing clear yellowish fluid.

Surgery has always been the method of choice and results are usually excellent with simple curettage after unroofing the cavity. In the larger cysts, or after pathologic fracture has occurred, slivers of bone may be implanted within the cavity.

X-ray therapy may be used and with satisfactory end results. However, a degree of uncertainty is inescapable and results are obtained much more slowly than after surgical treatment. Moreover, the hands and feet are to be regarded as regions where the late effects of irradiation may prove serious, and obliterating endarteritis is a particular hazard in these localities. For these reasons, surgery is generally to be preferred.

*Chondroma.*—Our series includes 15 chondromas (4 subungual exostoses); in addition there were 91 reported in the literature. These tumors consist largely of cartilage. Their common designation is central chondroma or osteochondroma, according to the direction of their growth; i.e., central or outward. Preferable and more descriptive are the terms enchondroma and echondroma. In the opinion of Gatewood, enchondromas arise from pre-existing cartilage and are probably congenital, due to an abnormal anlage in the intermediate cartilage of the bone involved. Some pathologists believe that they spring from islands of cartilage left in abnormal situations and hence may grow from the marrow in the phalanges, metacarpals, etc. Echondromas occur independently of any cartilaginous anlage and present themselves as an overgrowth arising where cartilage is normally present.

The central variety presents symptoms similar to those of a simple cyst or giant cell tumor, pathologic fracture being a common first symptom. While the roentgenographic appearance also presents features of

\*Coley, Bradley L., and Higinbotham, Norman L.: Surgical Treatment of Giant Cell Tumor, *Ann. Surg.* 103: 821, 1936.

both, as a rule they appear more multiloculated. The trabeculations are coarser and usually the entire shaft of the bone is involved. Irradiation therapy has been tried with success in a number of cases, but as they are particularly radioresistant prolonged treatment is required. One case in our series did not present roentgenographic evidence of healing until four and one-half years after the first treatment. Operation is preferable and is similar to the conservative operation for giant cell tumor; namely, thorough curettage, canterization with zinc chloride, and primary wound closure (Fig. 6). It is important to remove all traces of tumor tissue, as this type of tumor is prone to recur if not

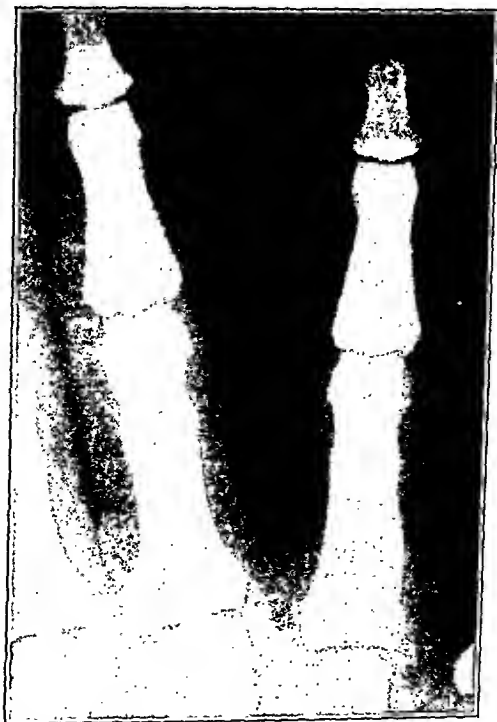


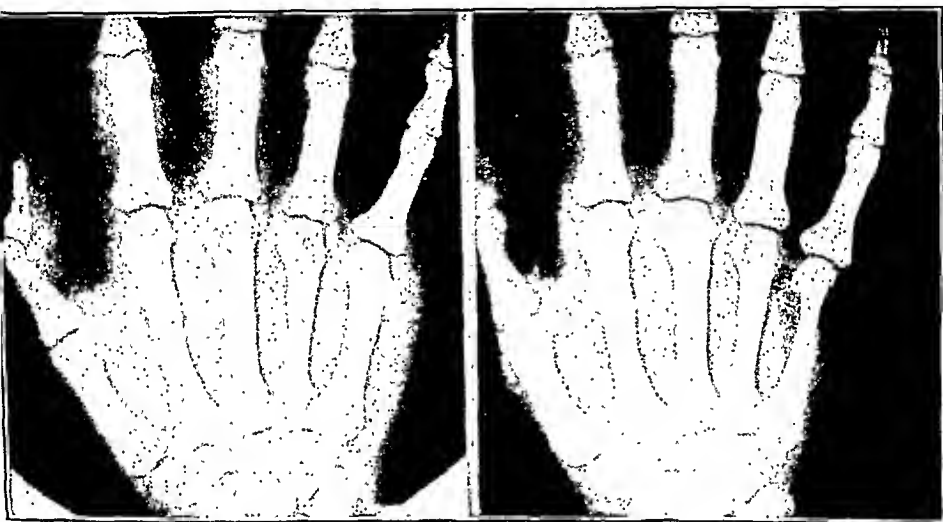
Fig. 6.—Case 17. Central chondroma of proximal phalanx of fourth finger. Male, aged 30 years. Curettage, cauterization and primary wound closure. No recurrence after two years.

adequately removed. As in cysts, small tibial bone grafts may be advisable when there has been much destruction or when pathologic fracture has occurred. We obtained an excellent result in the proximal phalanx of the ring finger with this latter procedure.

Eccchondromas are more apt to produce symptoms of pressure, due to their bony outgrowth, and frequently their first symptom is the detection of a bony protuberance. They are seen in the roentgenographs as definite bony outgrowths, usually with a broad base. Irradiation therapy has been tried, but it effects little, if any, regression in the

size of the tumor, due to its radioresistance. If they are causing symptoms, they should be removed by operation, care being taken to remove with the chisel a generous wedge-shaped portion at the base. Again complete removal is essential, as they are prone to recur if inadequately excised. One case in our series recurred twice and a third operation was necessary for complete relief (Fig. 7). Four other cases in our series showed excellent results following wide local excision.

Undoubtedly subungual exostosis should be grouped with the latter condition. We had 4 cases, all occurring as pyogenic granulomas of the great toe (Fig. 8). Our cases are grouped under the diagnosis of chondroma in Table II; whereas, the larger number occurring in the



A.

B.

Fig. 7.—Case 7. A, Osteochondroma (exostosis) of the fifth metacarpal. Female, aged 24 years. Excision. Recurred eight months later. Second excision. Recurred two years later. Third excision. B, Result 1½ years after third operation.

literature appears under the diagnosis of exostosis in Table III. According to Davidson, the patient first notices that the nail is being slowly raised from the usual flat position, and then there appears a hard growth from beneath the nail which pushes the nail backwards. The growth increases gradually in size until the nail becomes almost vertical in its axis. Mason states that the condition is most common in the foot (usually in the great toe) and that there are only a dozen cases reported as occurring in the hand (usually in the index finger). The roentgenographs generally show a characteristic bony outgrowth, but occasionally they may be negative if ossification has not occurred (Kurtz). Mason recommends removal with the least possible damage to the nail bed. Some authors recommend removal of the nail and removal of the growth with chisel and gouge, cauterizing the base

with phenol. Lapidus describes a more radical operation, employing a U-shaped incision, resecting the nail, and then resecting the distal half of the distal phalanx. He uses a long posterior and a short anterior flap. Any of these procedures may be employed, depending upon the size of the growth and the conditions present in the individual case.



FIG. 8.—Case 39. Subungual exostosis of big toe. Female, aged 16 years. Resection of distal half of nail, excision of exostosis, and base cauterized with zinc chloride. Pinch grafts to denuded area. Excellent result. No recurrence three years later.

*Myxoma*.—While our series contains no example of pure myxoma, 11 were found reported in the literature. The symptoms, signs, and roentgenographic appearance closely resemble those of chondromas and cysts. The differential diagnosis is extremely difficult and usually can be made on histologic examination alone. The operative or preoperative diagnosis is extremely important, however, because, as Kahn points out, these tumors require special treatment and are the most transplantable of all tumors. Thorough curettage must be employed and cauterization

is essential, as these tumors are extremely prone to recur. In this event Bloodgood recommends amputation.

Not infrequently chondromatous and myxomatous elements are mixed in the one tumor, producing a chondromyxoma. Some of these have been included under chondromas and others under myxomas in Table III, depending upon the author's description. The more the myxomatous element predominates, the more requisite it is to treat them as pure myxomas.

One must always bear in mind the grave possibility that a chondroma, myxoma, or chondromyxoma may undergo malignant transformation. It is for this reason that, however minor the symptoms, we believe with Campbell that they should be removed by operation at the earliest possible moment.

*Calcaneal Spurs.*—No examples of this condition have come to our attention in the Bone Tumor Clinic, as they are a not uncommon orthopedic problem dealt with by orthopedic surgeons. There are 205 cases reported in the literature. They are more common in the male and are often bilateral. The symptoms are usually acute and begin with pain in the heel, sometimes accompanied by swelling, so that the patient walks on his toes and forefoot with a characteristic gait. The acute attack may subside, but it is prone to recur, each subsequent attack being more prolonged. There is definite tenderness over the tubercle of the os calcis and roentgenographs show a characteristic exostosis. Formerly this condition was always attributed to gonorrhea, but actually this infection probably accounts for very few cases. It has been amply demonstrated that calcaneal spurs may be due to trauma, subacute gout, rheumatism, excessive standing, tuberculosis, or syphilitic epiphysitis (Warrack). Probably those due to gonorrhea and other infections occur as a local periostitis in which new bone is laid down and with each exacerbation additional layers of bone are deposited, the final result being a nodular mass of bone known as a spur (Lloyd).

Meisenbaek believes that spurs are actually bone formation and not a periostitis. Openshaw describes them as an overgrowth of the tubercle on the under surface of the os calcis, where the abductor minimi digitorum and the flexor brevis digitorum muscles attach. The treatment consists of general and local measures. The primary focus of infection must be sought for and dealt with. Meanwhile, a cushioned heel should be tried in the shoe. If the painful heel continues, operation for removal of the spur is indicated, and about 30 per cent of the cases will require operation. Simple excision with a chisel is usually sufficient. In more advanced cases larger incisions are required to expose the tubercle more adequately and after removing the spur with a chisel, the base is curetted and touched with carbolic acid. Steindler's operation is indicated in recurrent cases. Lloyd stresses the importance of always excising the bursa that forms, and Chang describes a modified operation



with phenol. Lapidus describes a more radical operation, employing a U-shaped incision, resecting the nail, and then resecting the distal half of the distal phalanx. He uses a long posterior and a short anterior flap. Any of these procedures may be employed, depending upon the size of the growth and the conditions present in the individual case.



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only 609 cases, one-third of which were subcalcaneal spurs. While the symptoms and signs are similar to those of tumors in other parts of the skeleton, the roentgenograph reveals dissimilar pathognomonic features. Aspiration biopsy is an important diagnostic aid. The treatment is essentially the same as that indicated for tumors of other bones. The ultimate prognosis, on the whole, would seem to be more encouraging. Finally, we would reiterate the dictum that persistent pain in the bones of the hands and feet, as in any bone, is an important first symptom and should be regarded with deep suspicion as indicating the possible existence of a primary bone tumor.

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in which a fascial transplant is placed over the denuded area after excision of the spur. Postoperative roentgenographs should be taken in order to be sure of complete removal of the spur.

Liberson employed deep x-ray therapy with gratifying results in 31 cases of painful heel, all of the gonorrheal type. This method of treatment merits a more extensive trial.

*Osteoid Osteoma.*—In 1932 Jaffe and Mayer described an osteoblastic osteoid tissue-forming tumor of the fourth metacarpal in a 15-year-old girl, and in 1934 Jaffe described 5 additional cases of a similar nature, 3 of which involved the bones of the hands and feet. They state that this tumor presents some features common to osteogenic sarcoma, but that it shows a benign behavior. It is well encapsulated, but capable of malignant transformation. It is usually diagnosed as inflammatory, but no pus is found at operation. On microscopic examination there are no features to suggest an inflammatory origin. All their cases were operated upon, the cavities cleaned out, and all had good results.

*Unclassified Sarcoma.*—There are 5 cases described in the literature as sarcoma without further differentiation as to type. Three were in the metatarsals, 1 in the cuboid, and 1 in the os calcis. We had 1 patient with an angiosarcoma of the metatarsal who died of multiple metastases one year after amputation of the foot.

*Metastatic Carcinoma.*—There are 2 cases of metastatic carcinoma in our series; 1 in the phalanx of a finger from a parotid tumor, and 1 in the astragalus from a hypernephroma. In addition we saw a metastasis to the phalanx of a finger from a breast carcinoma. There are 7 instances in the literature of metastatic involvement of the bones of the foot.

*General Diseases.*—The bones of the hands and feet may be involved in some of the generalized bone diseases. Thus, in von Recklinghausen's osteitis fibrosa cystica (hyperparathyroidism) these bones may show manifestations of the generalized decalcification and cystic formation. Achondrodysplasia with multiple cartilaginous exostoses also may involve the bones of the hands and feet. In osteopetrosis (marble bones, Albers-Schönberg disease) one of the characteristic features early in the disease is the dense, banded appearance of the phalanges, metacarpals, and metatarsals. Paget's osteitis deformans also may extend to these bones, and it is conceivable that melorheostosis also may progress to below the wrist and ankle. The extensive involvement of multiple or plasma cell myeloma also may include the bones of the hands and feet.

#### SUMMARY

In a series of 1,211 tumors of bone observed at the Memorial Hospital and the Hospital for Ruptured and Crippled, only 47 were found to involve the bones of the hands and feet. The entire literature contains

# Editorial

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## Heparin and Thrombosis

ATTENTION was first called to heparin in 1916 by Jay McLean, now a surgeon, who was at that time a medical student working in the laboratory of Professor W. H. Howell. This antieoagulant was obtained from the liver and was named heparin. Howell and his collaborators subsequently studied the distribution and chemical properties of heparin and succeeded in purifying it further. They pointed out its possible uses in clinical medicine. However, it was still considered unsafe for use in patients.

Professor Charles H. Best, of Toronto, became interested in heparin in 1929 and he visualized clearly its possible use in clinical as well as in physiologic work. With this in view, Charles and Scott began an attempt to obtain a highly purified preparation. They succeeded finally in obtaining from lung a crystalline barium salt of uniform potency. This was one hundred times as potent as the original crude material and was completely free of toxic properties. Charles found that the barium can be completely removed, that the heparin can be stored as a dry powder, and that a solution which can be sterilized by filtration can be made from this powder.

After having obtained a highly purified form of heparin, the physiologists and surgeons of the Toronto group began their studies on animals and patients. The results illustrate once again the value of animal experimentation in the advancement of clinical medicine and the great advantage of cooperative research when a problem needs to be attacked from various viewpoints. It was observed that heparin is effective when administered subcutaneously as well as when introduced intravenously. The best procedure in its administration was thought to be to give a small dose intravenously and to follow this with a constant intravenous injection. The clotting time of the blood in this way could be set at a chosen level and maintained there for long periods. In both experimental and clinical work, approximately 40 units of heparin per kilogram of body weight were given intravenously and this was followed with a continuous injection of approximately 30 units per kilogram an hour. The clotting time was usually maintained at from twenty to thirty minutes.

Many significant experiments were performed on animals, only a few of which will be mentioned. The effects upon the mixed thrombus, which is formed when veins are injured by mechanical or chemical means, were studied. The thrombus formation which was associated usually

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# Editorial

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After having obtained a highly purified form of heparin, the physiologists and surgeons of the Toronto group began their studies on animals and patients. The results illustrate once again the value of animal experimentation in the advancement of clinical medicine and the great advantage of cooperative research when a problem needs to be attacked from various viewpoints. It was observed that heparin is effective when administered subcutaneously as well as when introduced intravenously. The best procedure in its administration was thought to be to give a small dose intravenously and to follow this with a constant intravenous injection. The clotting time of the blood in this way could be set at a chosen level and maintained there for long periods. In both experimental and clinical work, approximately 40 units of heparin per kilogram of body weight were given intravenously and this was followed with a continuous injection of approximately 30 units per kilogram an hour. The clotting time was usually maintained at from twenty to thirty minutes.

Many significant experiments were performed on animals, only a few of which will be mentioned. The effects upon the mixed thrombus, which is formed when veins are injured by mechanical or chemical means, were studied. The thrombus formation which was associated usually

with a given injury did not occur when the insult was followed by the administration of heparin for seventy-two hours. Other experiments showed this to be true in the coronary arteries of the heart as well as in the peripheral veins. The white thrombus is the nucleus from which the mixed thrombus grows, and for this reason the Toronto group determined the effect of heparin on the formation of white thrombi. By allowing blood to flow over glass and cellophane tubing, it was found that heparin prevented the formation of thrombi which usually appear under these circumstances. Dr. D. W. G. Murray found that the percentage of successful end-to-end blood vessel anastomoses was considerably higher in the instances in which heparin was used. There is no doubt that nontoxic heparin will be a most valuable addition to the study of many problems in the laboratory, such as the anastomoses of blood vessels, transplantation of organs, exchange transfusions, and determinations of the rate of blood flow.

It is uncertain whether heparin is a normal constituent of the blood and whether it is the normal anticoagulant. Its wide distribution in the body suggests that it serves a physiologic function. There is excellent evidence that heparin is responsible for the markedly prolonged coagulation time of the blood in anaphylactic and peptone shock. Waters, Markowitz, and Jaques obtained from the blood of the shocked animal much more heparin than can be detected in the blood of the normal animal while the heparin content of the liver in shock was decreased.

Following the obtaining of highly purified preparations of heparin, clinical investigations were begun by Dr. Murray and associates in Toronto and by a number of workers in Sweden. Most of their efforts thus far have been centered upon attempts to prevent postoperative thrombosis and embolism. The importance of this condition is illustrated by the fact that approximately 6 per cent of the deaths following operations are due to massive pulmonary embolism and probably a larger percentage of the instances of pneumonia and lung abscesses may be due to smaller emboli. It is difficult to assess the value of heparin or any other therapeutic means as a preventive of postoperative thrombosis, but it may be said that the results thus far are encouraging and there have been no untoward experiences. It has been used by Murray without a fatality in a fairly large number of patients in the after-treatment of prostatectomy, splenectomy and other operations in which thrombosis and embolism are common. The intravenous administration of heparin is begun two or more hours following the operation and is continued for at least several days. It should be stated, however, that good results have been obtained by Baneroff and others by the use of a prophylactic regimen including the intravenous injection of sodium thiosulfate, large quantities of fluid by mouth, and the restriction of fats and carbohydrates in the diet.

As new findings are unearthed, it seems likely that heparin may be indicated in a variety of clinical conditions and operations. Among these may be included blood vessel anastomoses, peripheral embolism and embolectomy, phlebitis, coronary thrombosis, cerebrovascular thrombosis, and blood transfusions. Heparin may be used in the latter procedure either by adding it to the blood as it is collected or by injecting it into the donor. In the anastomoses of blood vessels, regional as well as general heparinization may be used. If the problem of the homotransplantation of organs is ever solved, it is probably there that heparin will find its greatest field of usefulness. Deterrents to the more general use of heparin at the present time include the discomfort to the patient of continuous intravenous injection, the increased nursing care and the price of the heparin. It costs about \$80.00 per patient if the blood of an adult is to be rendered incoagulable for several days. However, if time and additional work substantiate the findings referred to already, it is likely that most of these objections can be overcome. If the demand for heparin increases, the laboratories probably will be able to reduce the price. Furthermore, some bright worker probably will synthesize this substance. In the meantime, it should be determined whether or not heparin interferes with the healing of incisions and with the normal responses of the body to infection. Furthermore, the contraindications, if any, to its use should be established.

—*Alfred Blalock, M.D.*  
Nashville, Tenn.



# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## BEZOARS AND CONCRETIONS

A COMPREHENSIVE REVIEW OF THE LITERATURE WITH AN ANALYSIS OF  
303 COLLECTED CASES AND A PRESENTATION OF 8 ADDITIONAL CASES

MICHAEL DEBAKEY, M.D., AND ALTON OCHSNER, M.D.,  
NEW ORLEANS, LA.

*(From the Department of Surgery, School of Medicine, Tulane University)*  
*(Continued from the December issue.)*

*Diagnosis.*—The diagnosis of bezoars is not difficult if the condition is borne in mind. The relative rarity of these cases is conducive to the usual inadvertency or negligent inconsideration of the attending physician for the possible presence of these intragastric foreign bodies, thus forming the basic difficulty in their diagnosis. If for no other reason than as a reminder, their occasional presentation is thoroughly justified. Once the condition is suspected, the establishment of a correct diagnosis should be relatively simple.

In considering the diagnostic basis of trichobezoars, it should be recalled that a careful interrogation into the patient's previous habits in early childhood or adolescence frequently will elude the suggestive clue of trichophagia. Whereas the patient usually denies this hair-eating custom, it can usually be obtained from the parents or relatives. This was possible in over one-half of the collected cases (Graph VI). The great majority of these patients are girls or young women. This is demonstrated clearly by the series of collected cases, in which over 90 per cent were females and over 80 per cent were under the age of 30 years (Graphs III and IV). The presence of characteristic clinical manifestations, such as a rather large, firm, freely movable epigastric mass accompanied by some pain, nausea and vomiting, and anorexia, weakness, and loss of weight, is corroborative evidence. In the collected cases these symptoms and signs were prominently present. Fever is conspicuously absent. The presence of long strands of hair in the stools or in the gastric contents is confirmatory evidence. Usually there is a slight secondary anemia with a mild leucocytosis. Such a clinical picture, together with the characteristic fluoroscopic and roentgenologic findings previously described, will justify a diagnosis of trichobezoar. Whereas formerly in the absence of systematic roentgenologic examinations the diagnosis was usually made during the exploratory operation, at present, with the almost ubiquitous use of roentgenography, the lack of a correct preoperative diagnosis is indicative of misfeasance on the part of the physician.

The diagnosis of diospyrobezoars and other phytobezoars is also not attended with considerable difficulty if the condition is kept in mind. Again a careful inquiry into the patient's previous eating habits will often elicit the possibility. Thus, over 80 per cent of the collected cases of diospyrobezoars including the authors' gave a history of persimmon ingestion (Graph VI). In contrast to trichobezoars, approximately 80 per cent of the patients with phytobezoars are of the male sex and over 30 years of age (Graphs III and IV). Characteristically the clinical manifestations consist of a freely movable, firm abdominal mass usually located in the epigastrium and readily displaced beneath the left costal margin, associated with some pain or tenderness, nausea and vomiting, and moderate weakness or loss of weight. Constipation or diarrhea occurs in about one-third of the cases. Fever is prominently absent. If in addition to these findings there is a very slight secondary anemia and a mild leucocytosis, one should be even more suspicious of a phytobezoar. Gastric analysis reveals little more than probably a slight hyperacidity and stool examinations are not significant. However, in the presence of such a clinical picture the characteristic fluoroscopic and roentgenographic appearances previously described should definitely establish the diagnosis.

As an added diagnostic procedure, Moersch and Walters<sup>223</sup> recently have advocated direct visualization by means of gastroscopy. Whereas this undoubtedly is a valuable diagnostic aid, at present its usefulness is limited because there is required necessarily a special instrument and a high degree of skill.

The possibility of such complications as intestinal obstruction and gastroduodenal ulceration with consequent hemorrhage, perforation, and peritonitis always should be borne in mind. Obviously these complications assume different but characteristic clinical manifestations and therefore render the diagnosis of the original condition more perplexing. However, in the presence of such an eventuality the diagnosis of the complication is certainly more important.

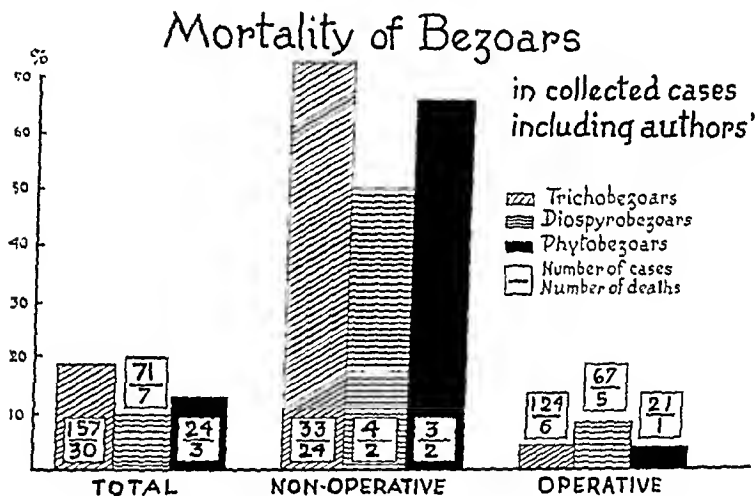
*Prognosis.*—The prognosis in bezoars depends primarily upon the presence or absence of two factors: (1) the institution of adequate therapy, and (2) complications.

That the institution of proper therapy is an important factor in the prognosis is readily evinced by the fact that the mortality in the non-operative collected cases of trichobezoars, diospyrobezoars, and other phytobezoars is 72.7 per cent, 50 per cent, and 66.6 per cent respectively, in contrast to the corresponding incidences in the operative cases of 4.8 per cent, 7.4 per cent, and 4.7 per cent (Graph VII). The significance of complications in the prognosis is clearly demonstrated by the fact that, whereas the mortality in the collected cases of trichobezoars and phytobezoars with complications is 53.1 per cent and 18.7 per cent respectively, in those cases without complications these corresponding

figures are 10.4 per cent and 2.1 per cent (Graph VIII). The total mortality in the collected cases of trichobezoars, diospyrobezoars, and phytobezoars, including ours, was 19.1 per cent, 9.8 per cent, and 12.5 per cent respectively (Graph VII).

Curiously enough the operative mortality in trichobezoars has not been diminished during the past three decades since Matas' publication. Whereas, in 1914, according to Matas, there were 2 deaths (4.1 per cent) in 48 cases operated upon, at present of 124 cases operated upon 6 (4.8 per cent) died.

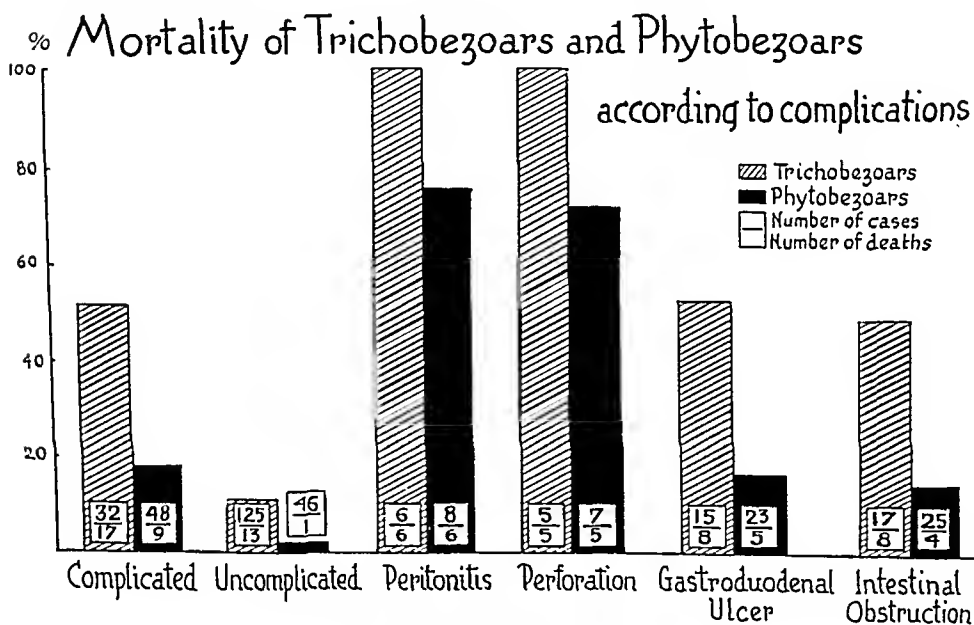
An analysis of the cause of death in the collected cases of bezoars is significant. It will be observed from Graph IX that intestinal obstruction occurred in 17 (10.8 per cent) of 156 collected cases of trichobezoars and 25 (26.5 per cent) of 94 collected cases of phytobezoars



Graph VII.—Comparative mortality rates based upon 252 collected cases of bezoars, including those of DeBakey and Ochsner.

including ours. Whereas of the 17 cases of trichobezoars, 8 (47 per cent) died; of the 25 cases of phytobezoars only 4 (16 per cent) died. This considerable difference in mortality rates in the two types of bezoars is probably due to the fact that the patient with trichobezoar is usually in a weaker and more exhausted condition by virtue of a longer duration of the original, larger intragastric foreign body. In our series of 7 cases of phytobezoar, there were 3 (Cases 4, 5, 6) with intestinal obstruction. Two of these (Cases 5 and 6) were treated conservatively and 1 (Case 6) eventually passed the bezoar in the stool; whereas the other (Case 5), admitted in extremis, died within twenty-four hours. The third patient (Case 4) was operated upon on a service other than ours and the bezoar was removed through an enterostomy. The patient's progress was very satisfactory for four days postoperatively under a physiologically rational postoperative therapy. However, on the fourth postoperative

day this was discontinued and ice water, fruit juices, and sweetened soda water drinks were administered. The following day the temperature rose to  $103^{\circ}$  F., the pulse became rapid, there was marked abdominal distention, and the patient vomited everything administered. Enemas were given with no apparent relief in the distention. Under this regimen for four days the patient became progressively worse, then the heat tent and Wangenstein suction were applied, but by this time the patient was beyond even heroic measures and died the following day. Whereas it would be inopportune to attempt here a detailed discussion of metaplaparotomy therapy based on physiologic principles, it is worthy of emphasis because this case illustrates in such a tragic but strikingly significant manner the fallacious and even disastrous irrationality of



Graph VIII.—Graphic representation of mortality in collected cases of bezoars according to complications.

the postoperative administration of ice water, fruit juices, and sweetened soda water beverages. This has been discussed adequately in previous publications.<sup>330-332</sup> It is our firm conviction that even upon the day following the development of marked abdominal distention, hyperpyrexia, and vomiting, had the administration of iced and sweetened beverages been discontinued and the patient again placed on the more rational postoperative therapy consisting of (1) Wangenstein suction, (2) pleboeclysis of glucose and saline, (3) heat tent over the abdomen, and (4) morphine, the outcome probably would have been different.

Fifteen (9.6 per cent) of the collected cases of trichobezoars and 23 (24.4 per cent) of the collected cases of phytobezoars were complicated by gastroduodenal ulceration (Graph IX). Whereas of the 15 cases

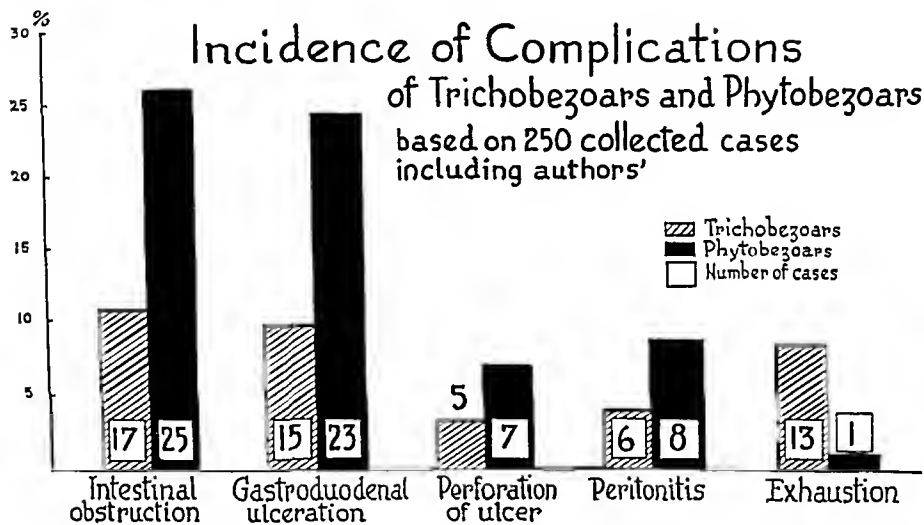
of trichobezoars with ulcers, 8 (53.3 per cent) died; of the 23 cases of phytobezoars only 5 (21.7 per cent) died (Graph VIII). These contrasting mortality rates in the two types of bezoars are due probably in great measure to the difference in the intragastric contents. The foul, putrid material characteristically associated with trichobezoars undoubtedly contains more virulent pathogenic organisms than the relatively sterile intragastric contents of phytobezoars. This is further corroborated by the fact that all of the 5 cases of trichobezoar ulcers that perforated died; whereas, of the 7 cases of phytobezoars with perforated ulcers only 5 (71.4 per cent) died (Graph VIII). In this regard the fact that all of 6 cases of trichobezoars that developed peritonitis died and only 6 of the 8 cases of phytobezoars with peritonitis died is significant (Graph VIII).

The complications resulting from the various types of bezoars are due primarily to: (1) interference with the normal physiologic activity of the gastrointestinal tract, namely, obstruction and exhaustion or inanition; and (2) traumatic irritation to the stomach and bowel wall and its consequences, mucosal erosion, ulceration, perforation, and peritonitis. The occurrence of such complications is readily comprehensible upon the realization that bezoars, in the final analysis, are simply foreign bodies in the gastrointestinal tract. Obviously, the complication produced depends essentially upon the primary mechanical effect of the foreign body upon the normal physiology of the stomach and intestines. Thus, a trichobezoar may gradually grow to such enormous proportions that the stomach can no longer compensate for its presence and additional space required by food ingested. The arrival of this degree of tolerance is then manifested usually by vomiting and the patient actually starves to death of inanition and exhaustion unless appropriate therapy is instituted. In a series of 156 collected cases of trichobezoars this eventuality occurred in 13, an incidence of 8.3 per cent. On the other hand, this complication occurred in only 1 of 94 collected cases of phytobezoar (Graph IX). This difference may be accounted for by the fact that the latter type of bezoar is more likely to be of smaller dimensions and less likely to increase in size.

Another mechanical effect of bezoars is the possibility of obstructing the lumen with the consequent manifestations of mechanical ileus. This forms the most frequent complication in both types of bezoars. In trichobezoar this is usually due to the breaking off from the original hair-ball in the stomach of a small portion which so frequently extends through the pylorus and into the duodenum. That this may very likely occur is readily understood by a close examination of these bezoars. For example, in the authors' case the rather long extension into the duodenum was connected to the original trichogenous intragastric mass by a more narrow and less intact area corresponding to the position of the pylorus (Fig. 1). That such small sections do break off is demonstrated by the

fact that not infrequently they are passed in the stools. However, in some instances they become lodged in the intestine, most frequently in the terminal ileum, and then produce the characteristic manifestations of ileus. Of the 156 collected cases, this occurred in 17 (10.8 per cent). As might be expected, this complication is considerably more frequent in phytobezoars, as is shown by the fact that of the 94 collected cases there were 25 (26.5 per cent) with this complication (Graph IX). In our series of 7 cases intestinal obstruction developed in 3 (42.8 per cent). Its greater frequency of occurrence in phytobezoars is due to the fact that they are more likely to be multiple, of harder consistency, and more irregular in surface.

The complications produced by the traumatic influence of these foreign bodies is usually manifested by gastroduodenal ulceration and



Graph IX.—Comparative incidence of complications in bezoars based on 250 collected cases of bezoars, including the cases of DeBakey and Ochsner.

consequent hemorrhage, perforation, and peritonitis. Again, as might be predicted, gastroduodenal ulceration occurs much more frequently in phytobezoars than in trichobezoars. Whereas, of the 156 collected cases of trichobezoars, this complication was present in only 15 (9.6 per cent); of the 94 collected cases of phytobezoars it occurred in 23 (24.4 per cent) (Graph IX). Only 1 (14.2 per cent) of our series of 7 cases had this complication. The most obvious explanation for the higher incidence of gastroduodenal ulceration in phytobezoars is that their harder consistency and more irregular surface have greater potential traumatic influence. Grossly the ulcers complicating bezoars are similar in every respect to peptic ulcers as is illustrated in our case (Fig. 12). Of even greater interest is the characteristic location of these ulcers, which opens a rather intriguing speculative consideration of the etiology of peptic ulcer. Of 10 cases of trichobezoars with ulcers in which the

location was stated, 8 were on the lesser curvature and 2 on the greater. Of the 19 collected cases of phyto bezoars including ours, 15 were on the lesser curvature and 4 were on the greater. In our case the ulcer was situated on the greater curvature (Fig. 13). Thus, of the total 29 cases, 23, or approximately 80 per cent, were located on the lesser curvature, an incidence which corresponds fairly closely with that of gastric ulcer. The question which immediately arises is why should ulceration occurring in these cases develop in such a characteristic location and one which corresponds so closely with the site of the ordinary gastric ulcer. It would appear that a foreign body, such as a trichobezoar, forming an almost complete cast of the stomach, should produce an evenly distributed trauma to the mucosa and not a concentrated irritative action to a small area. Moreover, it certainly cannot be con-

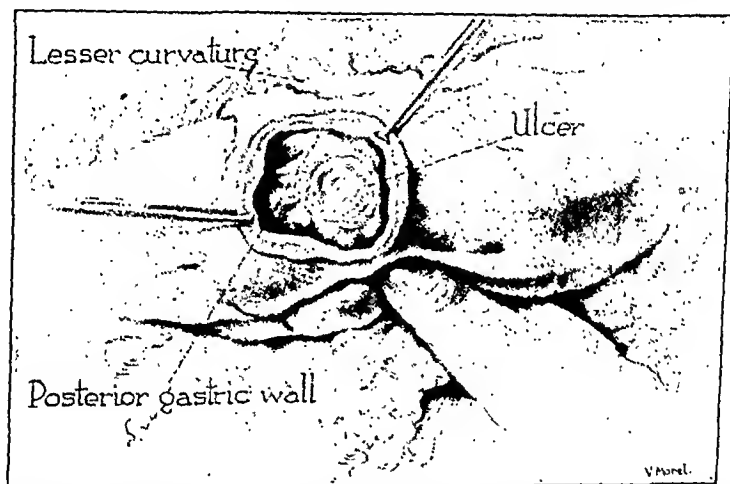


Fig. 12.—Drawing of chronic ulcer along greater curvature of stomach as seen through gastrotomy incision at time of operation as described in Case 7. Grossly this ulcer resembled the ordinary gastric ulcer in every respect.

sidered a coincidence nor can one argue that these individuals would develop ulcers anyway in the absence of bezoar, for the incidence is entirely too high. The occurrence of these ulcers in this strictly limited localization with such striking uniformity almost forces the admission that the mechanism of formation must necessarily closely parallel that of ordinary gastric ulcer. Indeed, it would appear to lend support to the significance of the mechanical factor as propounded by Aschoff,<sup>333</sup> whose conception was based upon a comprehension of the function of the so-called *magenstrasse* or gastric pathway which is assumedly the route by which gastric chyme is propelled from the pylorus into the duodenum. The presence of bezoars further enhances the mechanical or traumatic factor by interference with proper emptying of the stomach, thus creating first, gastric retention which augments and prolongs gastric motility and gastric acid secretion; and second, prevention of

normal duodenal regurgitation which is the major factor in the neutralization of gastric acidity. Furthermore, the characteristic situation of these ulcers would seem to emphasize the significance of tissue susceptibility as a predisposing factor in the genesis of ulcer. That the lesser curvature of the stomach (*magenstrasse*) has an inherent vulnerability or an intrinsic quality of susceptibility to peptic ulceration has been shown by numerous investigators. Morton<sup>334</sup> observed that after "surgical duodenal drainage" procedures, ulcers along the greater curvature healed; whereas, those on the lesser curvature became chronic. This greater sensitivity of the mucosa along the lesser curvature to peptic ulceration has been demonstrated convincingly by Ochsner, Gage, and

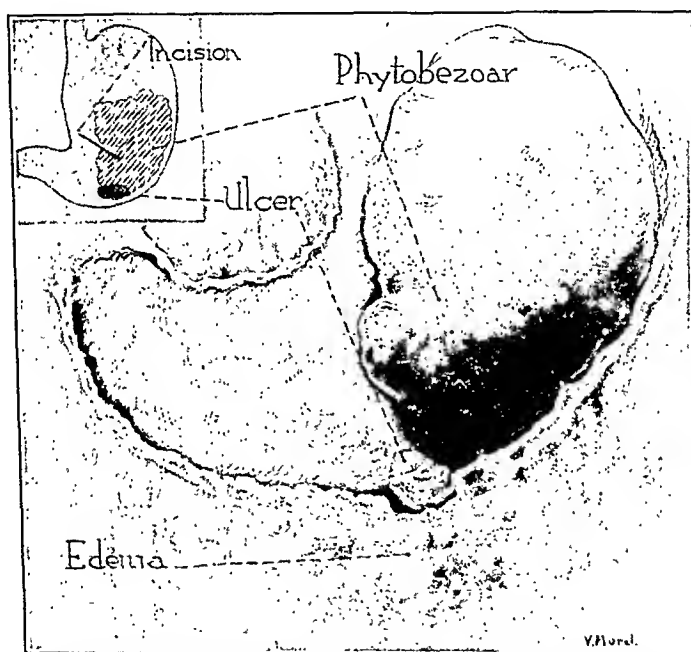


FIG. 13.—Drawing to illustrate relative size of diospyrobezoar removed at operation in Case 7 and to show the relative position of the ulcer along the greater curvature of the stomach.

Hosoi.<sup>335, 336</sup> Thus, the development of these characteristic ulcers in the presence of bezoars may be explained to some extent on the basis of the two factors; namely, tissue susceptibility and mechanical or traumatic.

However, we are fully cognizant of the fact that, whereas these two factors may play the most conspicuous roles in the genesis of these bezoar ulcers, they cannot be considered as the only operating factors. Obviously, if this were true, the incidence of bezoar ulcer would be considerably higher than 15.2 per cent. Moreover, on this basis it would be difficult to explain satisfactorily the absence of ulceration in cases of bezoars existing as long as ten years or more. Undoubtedly, here as in



peptic ulceration in general no single factor can be held solely responsible for their development. A recent recapitulation of the voluminous clinical and experimental investigations clearly indicates that ulcer is the result of a "tessellation of factors."<sup>337</sup> We have expounded previously a thoroughly rational understanding of the physiologic principles involved in the development and maintenance of peptic ulceration and are of the opinion that the occurrence of these bezoar ulcers is not only satisfactorily explained on this basis but even lends support to the exposition.<sup>337-341</sup> This concept maintains that ulcer is established by the summation of two groups of factors: (1) the *predisposing*, which are inherent and therefore uncontrollable; and (2) the *precipitating*, which are controllable. The former group is composed of: (a) tissue susceptibility, which has been alluded to previously and which may be defined as an inherent vulnerability of certain portions of the gastrointestinal tract, such as the lesser curvature of the stomach (*mogengeschwulst*), the duodenal cap, etc., to the digestive eroding effect of the acid gastric juice; and (b) constitutional, which is extremely difficult to define and must be considered as an ingrained susceptibility of certain individuals to gastroduodenal ulceration. Whereas the former innate characteristic is present in all individuals, the latter exists only in those individuals who develop ulcer in the presence of the precipitating factors. Thus, both these predisposing factors, i.e., tissue susceptibility and constitutional predisposition, may be present in an individual without peptic ulcer necessarily developing. However, ulceration does occur if to this predisposing group there are added the precipitating factors which consist of (a) chemical, (b) mechanical or traumatic, and (c) infection. On this basis a ready and satisfactory explanation exists for the development of ulcers in that group of bezoar patients having this complication (15.2 per cent) as well as those in which ulcers do not occur (84.7 per cent). The precipitating factor exists in both groups but the constitutional factor is present only in the former. In order for ulcer to develop, both factors must necessarily be present. The fact that the simple removal of the bezoar, or to state it differently, the removal of the precipitating factor, is almost invariably followed by disappearance of the ulcer further corroborates this hypothesis.

These ulcers in bezoars may be complicated further by perforation and peritonitis. Curiously enough, the incidence of perforation in the ulcers of both types of bezoars is about the same. Of the 15 collected cases of trichobezoars with ulcers, 5 (33.3 per cent) perforated and of the 19 collected cases of phytobezoars with ulcers 7 (36.8 per cent) perforated. Whereas death followed all the perforated cases of trichobezoars, this eventuality occurred in only 5 (71.4 per cent) of the phytobezoars (Graph VIII). This may be explained probably by the fact that the intragastric contents of trichobezoars, characteristically foul, are more likely to harbor pathogenic organisms.

*Treatment.*—The treatment of bezoars and concretions is essentially surgical and consists of the operative removal of the foreign body usually from the stomach and occasionally from the intestines. Conservative measures, consisting of the administration of dilute hydrochloric acid<sup>342</sup> or external massage<sup>189</sup> in an attempt to cause chemical or mechanical disintegration of the foreign body, have been suggested but cannot be approved. Surgical intervention is obviously the only rational therapeutic procedure. This is further corroborated by the self-evident results of the statistical analysis of the collected cases. Thus, whereas the mortality in the nonoperative cases of trichobezoars, diospyrobezoars, and other phytobezoars is 72.7 per cent, 50 per cent, and 66.6 per cent respectively, these corresponding figures in the operative cases are 4.8 per cent, 7.4 per cent, and 4.7 per cent (Graph VII).

It is considered unnecessary as well as inexpedient to attempt here a detailed discussion of the operative technique. However, it is adjudged desirable to direct attention to a few salient technical factors. The type of abdominal incision is of no great moment but should permit an adequate approach to the stomach. Particular emphasis is attached to the care with which intraperitoneal exclusion is done before opening the stomach, especially in trichobezoars. Obviously the gastrotomy incision should be made on the anterior wall and at right angles to the longitudinal axis of the stomach. Because of the frequent enormous size of trichobezoars, it is usually necessary to make a rather large opening in the wall of the stomach. Also, due to the long duration of these intragastric trichogenous masses and the resultant stasis, fermentation, and decomposition, there is usually an associated slimy, foul, putrid material. For this reason special precautions should be taken in the removal of these foreign bodies to prevent possible contamination of a virgin peritoneal cavity. Because frequently there is extension of the hairball through the pylorus and for some distance into the duodenum, the operator should exercise particular care in extracting the entire foreign body.

In considering the operative removal of phytobezoars, it is important to realize the not infrequent concomitant occurrence of two or more intragastric masses as well as the occasional presence of a mass in the intestines. It will be recalled that this occurred in 17.5 per cent and 4.4 per cent respectively of the collected cases of phytobezoars including ours. For this reason a thorough exploration of the stomach is imperative in order to be absolutely certain that all the foreign bodies have been removed. That such a precaution is not stressed unduly is demonstrated clearly by the case of Outten,<sup>190</sup> the case of Davis reported by Hart,<sup>196</sup> and our Case 8. The case reported by Outten, in 1894, is amazingly similar to our Case 8 which was not treated in our service. In both cases there were two intragastric diospyrobezoars. Whereas in Outten's case the second bezoar was recognized and removed through a

second gastrotomy incision before the abdominal wound was closed, in the case reported by us a subsequent operation was necessary. That such a mistake should be repeated forty-four years later is an ironic tribute to medical literary efforts.

Obviously, in the presence of such complications as intestinal obstruction and peritonitis, the institution of appropriate therapy must vary accordingly. The cases of bezoars associated with simple ulcers, i.e., nonperforative, merely require the removal of the foreign body. Because of the pathogenic nature of this type of ulcer, the removal of the traumatic factor usually is sufficient. Our Case 7 readily illustrates this fact. Whereas the ulcer in this case was grossly similar to the ordinary chronic gastric ulcer, following the removal of the diospyrobezoar, which was the traumatic factor, the ulcer apparently healed completely.

#### CASE REPORTS

**CASE 1.**—F. L., single, white, servant girl, aged 15 years. Admitted to Charity Hospital Jan. 23, 1935, complaining of vomiting.

For past three months patient has awakened regularly at 2 A.M. to vomit. During this same period of time she has been able to eat only small amounts every two hours. She has experienced slight epigastric discomfort and fullness. Since she began vomiting, she has noticed a large hard mass in upper abdomen. There has been rapid loss of weight recently and considerable weakness. No hematemesis and no constipation.

Patient admitted that as a younger child she used to chew and swallow her hair but at present only bites her nails. However, parents state that during the night while patient is fast asleep, she has been observed to seize her hair, tear it out, and place it into her mouth.

**Physical Examination.**—Patient is thin and pale. Weight, 82½ pounds. Neuropsychiatric survey "reveals every evidence of an inadequate personality plus a constitutional inferiority. Psychometric study shows middle grade morosity. Neurological examination negative." Temperature, pulse, and respiration normal. Significant findings are in the abdomen only. Inspection reveals a prominence extending from the upper midepigastrium and left hypogastrium diagonally downward to the lower right hypochondriac region. It is displaced downward on deep inspiration and palpable as a well-defined firm mass crescentic in shape, roughly suggesting a dilated stomach. It seems to extend from beneath the left costal margin to a point just below and to the right of the umbilicus. It can be readily moved in all directions. There is slight tenderness but no rigidity.

**Laboratory Studies.**—Wassermann, negative; urinalysis and blood chemistry, normal; R.B.C. count, 5,290,000; Hb., 75 per cent; W.B.C. count, 12,000; neutrophils, 86 per cent; small mononuclears, 11 per cent; large mononuclears, 3 per cent. Stool examination: Hair present in feces. Gastric analysis: Free HCl, 4; total acidity, 28. Roentgenographic examination: Fluoroscopic examination following ingestion of barium meal reveals no abnormalities in the esophagus. As the barium enters the fundus, it seems to hesitate and then splits into two layers flowing downward along the greater and lesser curvatures. This defect in the barium shadow is caused by a foreign body as there is no involvement of the walls of the stomach. The six-hour plate shows a greatly distended stomach and duodenum apparently containing a large hairball (Fig. 5).

**Preoperative Diagnosis.**—Trichobezoar.

Operation, Jan. 31, 1935: Upper right rectus incision. Upon exposing the stomach, it is evident that the tumor is intragastric and completely fills the entire stomach. Further exploration reveals the mass extending through the pylorus into the duodenum. The peritoneal cavity is carefully excluded by packing wet cloths around the exposed anterior wall of the stomach. An incision at right angles to the longitudinal axis of the stomach is made about the middle of its anterior wall. An immense slimy, foul-smelling hairball is found which so completely fills the stomach that it forms a perfect cast of this organ. By careful massage, traction, and manipulation, the mass, which extends into the second portion of the duodenum, is removed in its entirety (Fig. 1). The gastrotomy incision is then closed with three rows of sutures. The wound is closed in layers.

Patient's recovery was uneventful. On March 27, 1935, two months after operation, roentgenographic studies with barium revealed no filling defect in stomach or cap and no six-hour gastric residue. Stomach is normal in size.

*Specimen.*—Mass consists of firmly matted and closely packed dark brown long hair with a glairy, mucoid surface coating and an extremely foul odor. In contour it resembles a cast of the stomach and part of the duodenum. Particles of fat and other undigested food substances are intimately mixed with the hair. The mass weighs 750 gm. and measures, exclusive of the duodenal extension, 42 cm. along the greater curvature, 21 cm. along the lesser curvature, and 20 cm. in circumference at the fundus (Fig. 1).

CASE 2.—A. M., white, married male, laborer, aged 32 years. Admitted to Charity Hospital, Dec. 20, 1935, complaining of vomiting blood.

*Present Illness.*—Patient's illness began about one month prior to hospitalization with sudden onset of rather severe cramplike pain during hunger which was relieved following eating. These symptoms recurred every day for two weeks, then he began vomiting small amounts of blood and dark brownish to black material. This continued almost daily until Dec. 20, 1935, the day of admission to hospital, when he suddenly became very weak and vomited a large quantity of blood and passed tarry stools. The cramplike pains have persisted and he has experienced a weighty sensation in the epigastrium. Previously patient had no gastrointestinal disturbances.

*Physical Examination.*—Patient is thin, obviously in poor health, very weak and pale, apparently almost in shock. Temperature, normal; pulse, 100; and respirations, 28. Significant findings limited to abdomen. No abnormalities observed on inspection. Freely movable firm mass palpable in epigastrium. Slight tenderness but no rigidity present.

*Laboratory Examinations.*—Wassermann, negative; urinalysis, normal; R.B.C. count, 3,450,000; Hb., 60 per cent.

Roentgenographic examination after barium meal reveals negative shadow in stomach in region of incisura angularis which may be considered as possible polyp. The six-hour plate showed no gastric retention with the meal resting in terminal ileum and cecum.

Because of the secondary anemia, the patient was given two 500 c.c. blood transfusions before operation.

*Operation.*—Jan. 6, 1936, under ether anesthesia a left paramedian incision is made. Upon examination of the stomach a hard mass about the size of a fist is palpated. The stomach is delivered into the wound and the surrounding area carefully packed with wet cloths. Through a transverse incision made in about the middle of the anterior wall of the stomach a black, hard, oblong-shaped mass about 6 cm. in length and 4 cm. in width is removed. The gastrotomy incision is closed with three rows of sutures. The abdominal incision is closed in layers.

*Pathologic Report.*—The specimen consists of an oblong-shaped mass firm in consistency and dark brown to black in color, measuring  $6\frac{1}{2}$  cm. by 4 cm. by 4 cm. The

external surface is slightly irregular with clefts and pits (Fig. 2). On section the entire inner portion consists of amorphous light brownish material with a dark brownish seed near the center (Fig. 4). Microscopic examination further suggests that this is a phytobezoar, probably of persimmon origin.

The patient was discharged on Jan. 21, 1936, in good condition after an uneventful recovery.

**CASE 3.**—R. K., white male, electrician helper, aged 25 years. Admitted to Charity Hospital Aug. 12, 1936, complaining of epigastric pain, nausea, and vomiting.

**Present Illness.**—For several years patient has had vague gastrointestinal disturbances, but during past year condition has become worse rapidly and is manifested by weighty sensation and dull pain in the epigastric region. This is well-localized in character and almost constantly present, although the pain seems to be worse following meals and on assuming different positions. Nothing relieves the pain. During the past few months he has been conscious of a "lump in the stomach." Recently he has become nauseated and occasionally vomits after meals. Appetite is poor and he has lost twenty pounds in six months. No hematemesis or melena.

**Past History.**—States that when he was 10 to 14 years of age he ate large quantities of persimmons but has not eaten any since.

**Physical Examination.**—Patient is well-developed but undernourished. Temperature, pulse, and respiration normal. No significant findings except in abdomen.

**Inspection of abdomen** reveals no abnormalities. On palpation a firm mass about 6 to 8 cm. in diameter is felt in the epigastrium just above and to the left of the umbilicus. It is readily movable from side to side and can be pushed up beneath the left costal margin so that it disappears. It also moves when patient changes position. It does not necessarily move on respiration. There is very slight tenderness and no rigidity.

**Laboratory Examinations.**—Wassermann, negative; urinalysis and blood studies, normal.

**Röntgenographic examination** after barium meal: Fluoroscopic examination reveals foreign body in stomach. Gastrointestinal series shows a filling defect of the stomach which has the appearance of a food or hairball (Fig. 6). There is slight six-hour gastric residue.

**Preoperative Diagnosis.**—Phytobezoar.

**Operation,** Aug. 13, 1936. Under epidural analgesia, left paramedian incision is made. Upon exposing the stomach, an intragastric freely movable mass, firm in consistency and about the size of a fist, is readily palpable. The stomach with the mass is delivered into the wound and the operative field carefully excluded with wet packs. A transverse incision extending between the greater and lesser curvatures about 6 cm. in length is made in about the midpart of the anterior wall of the stomach. Through this incision by gentle manipulation a firm dark brown to black mass roughly oval to rectangular in shape is removed. The gastrotomy incision is closed with three rows of sutures. The abdomen is closed in layers.

**Pathologic Report.**—Specimen consists of a firm, hard, dark brownish mass with a slightly fermentative odor measuring 9 by 5 by 2½ cm. The surface is somewhat bosselated with some smooth areas. On section it appears to be composed of an amorphous, yellowish substance which on microscopic examination confirms the diagnosis of phytobezoar probably of persimmon origin.

Patient was discharged on Sept. 24, 1936, in good condition after an uneventful recovery.

**CASE 4.**—S. F., white, male, aged 10 years. Admitted to Charity Hospital Oct. 10, 1936, complaining of pain in right lower quadrant of abdomen.

**Present Illness.**—Began suddenly on Oct. 7, 1936, with rather severe colicky pain in right lower abdominal quadrant followed by nausea and vomiting. Had slight

diarrhea at onset but has been constipated since. Patient was given three doses of castor oil but vomited it on each occasion. The nausea, vomiting, and colicky pain have persisted with varying periods of relief. The vomitus is described as being bitter and greenish in color. Also complains of rather severe frontal and temporal headaches. Patient has no appetite and has become very weak since onset of illness. Subsequent questioning of parents reveals that he had engorged himself on persimmons a few days before onset of illness.

*Family History.*—Parents state that in 1931 an older brother of patient had similar clinical manifestations following ingestion of large quantities of persimmons and was relieved by operation.

*Physical Examination.*—Patient is well-developed but slightly undernourished, obviously ill, and suffering pain. Temperature, 100° F.; pulse, 120 per minute; and respiration, 36 per minute. Significant findings limited to abdomen which on inspection reveals slight distention. Liver and spleen are not palpable and no masses can be felt. There is moderate generalized tenderness and rigidity most marked in right lower quadrant.

*Laboratory Examinations.*—Wassermann, negative; urinalysis, normal; W.B.C., 11,700; neutrophils, 62 per cent; small mononuclears, 28 per cent; large mononuclears, 10 per cent; R.B.C. count, normal.

Diagnosis of intestinal obstruction probably due to phytobezoar of persimmon origin was made. Patient was treated conservatively by phleboeclysis of glucose and saline solutions, sedation, and surgical liquids for approximately one week with no evidence of improvement.

Operation, Oct. 18, 1936: Under ether anesthesia a right paramedian incision is made. Upon opening the peritoneal cavity a large quantity of peritoneal fluid escaped. The small bowel is markedly distended. Further exploration reveals a hard round mass in the terminal ileum about 10 cm. from the ileocecal junction which is obviously the site of obstruction. This loop of bowel containing the mass is delivered into the wound and carefully excluded from the peritoneal cavity by packs of wet cloths. A transverse incision is made in the ileum just over the mass and it is readily removed. The mass is dark brown in color, round with an irregular surface measuring about 5 cm. in diameter. The enterostomy opening is closed with three layers of suture. The appendix is examined, found to be acutely inflamed, and removed. The abdominal incision is closed in layers.

The immediate postoperative therapy consisted of: (1) Wangensteen suction, (2) phleboeclysis of glucose and saline solutions, (3) heat tent over abdomen, (4) nothing by mouth except water, (5) sedation by morphine gr. ½.

The patient's progress was very satisfactory for four days postoperatively until Oct. 23, 1936, when heat tent and Wangensteen suction were discontinued. At this time ice water, fruit juices, and sweetened soda water drinks were administered. The wound was also observed to be infected and drainage instituted. The following day there was marked abdominal distention; the temperature ranged from 102° to 103° F. and the pulse was 150 per minute. Patient continued to vomit everything given. Enemas were given with no apparent relief of the distention and the patient was obviously getting worse. The heat tent and Wangensteen suction were reapplied on Oct. 27, 1936, but the patient died the following day.

*Autopsy.*—Oct. 28, 1936: Significant findings limited to peritoneal cavity which contained a large amount of thick purulent yellowish exudate. The loops of bowel are adherent by thin fibrinous adhesions which contain localized collections of pus. Similar collections are above the liver, in the right and left iliac fossae, and in the pelvis. The side of the enterostomy appears intact in the ileum 10 cm. from the ileocecal valve with no evidence of leakage. The site of the appendectomy also reveals no evidence of leakage. The bowel is considerably distended, but there is no evidence of perforation. Within the stomach a round foreign body is found,

dark brown to black in color, measuring 5 cm. in diameter, having an irregular surface, and closely resembling the foreign body previously removed at operation. Subsequent microscopic and macroscopic examinations prove these masses to be phytobezoars containing persimmon seeds. The liver shows evidence of acute hepatitis and perihepatitis and the spleen has the characteristics of acute toxic splenitis. The postmortem diagnosis is: (1) generalized peritonitis, (2) acute intestinal obstruction caused by phytobezoar probably of persimmon origin, (3) sub-acute appendicitis, (4) acute toxic hepatitis and splenitis.

**CASE 5.**—Mrs. J. M., white married female, aged 50 years. Admitted to Charity Hospital Nov. 2, 1936, complaining of epigastric pain, nausea, and vomiting.

*Present Illness.*—Began suddenly on the morning of Oct. 28, 1936, following breakfast with severe cramplike pain in the epigastric region which was followed by marked nausea and vomiting. A physician prescribed castor oil which was repeated before her bowels moved with very little effect. Since then she has been constipated. The nausea and vomiting have persisted. The pain is not as severe, although it has never completely disappeared. She has become moderately distended and weak. The vomitus has recently become foul smelling.

*Physical Examination.*—Patient is well-developed, rather obese, apparently acutely ill. Temperature, 99° F.; pulse, 100 per minute; respiration, 26 per minute. Significant findings limited to abdomen, which on inspection is moderately distended with no visible masses or scars. The abdominal wall is very thick, making palpatory examination rather difficult. However, no masses could be felt and the liver and spleen are not palpable. There is slight generalized tenderness but no rigidity.

*Laboratory Examinations.*—Wassermann, negative; urinalysis reveals slight amount of albumin; red cell count is normal; blood culture, negative.

A tentative diagnosis of acute high intestinal obstruction is made, but operation is considered inadvisable because of patient's poor condition. Conservative therapy consists of Wangensteen suction, phlebotomy of glucose and saline solutions, heat tent over abdomen, and morphine sedation. However, patient rapidly became worse the next day and died twenty-four hours after admission.

*Autopsy:* Nov. 3, 1936: Significant findings limited to peritoneal cavity which contains a small amount of clear straw-colored fluid. The small bowel is markedly distended to a point about 65 cm. from the ileocecal valve below which the bowel appears normal. At this site a foreign body causing the obstruction is found in the lumen of the ileum. It is a firm, black, oblong-shaped, somewhat flattened mass having an irregular surface measuring 4 by 2½ by 2 cm. On section it consists of a light brown amorphous granular substance in which is imbedded a persimmon seed and what appears to be persimmon skin. There are a few vegetable fibers interspersed in the material. Subsequent examination further indicates this to be a phytobezoar of persimmon origin. At the site of obstruction the mucosa seems ulcerated and the bowel is congested and edematous. The liver and spleen present the characteristics of acute toxic hepatitis and splenitis.

Post-mortem diagnosis is: (1) acute intestinal obstruction due to a phytobezoar probably of persimmon origin; (2) acute toxic hepatitis and splenitis.

**CASE 6.**—A. C., colored male laborer, aged 37 years. Admitted to Charity Hospital Nov. 21, 1936, complaining of "locked bowels."

*Present Illness.*—On Nov. 16, 1936, five days previous to admission, patient suddenly developed cramplike pain in right lower quadrant. This has persisted with occasional periods of relief, although successive attacks have become more severe. Sometimes the pain radiates down towards the hypogastrium. Bowels have not moved since onset of pain in spite of purgatives. On day before admission immediately following meal he became nauseated and vomited the food ingested. Since then has vomited anything ingested.

*Physical Examination.*—Patient is fairly well developed but slightly undernourished, apparently dehydrated, and obviously ill. Temperature, pulse, and respiration are normal. Significant findings limited to abdomen which on inspection reveals visible peristalsis. There is moderate degree of distention and enlarged veins are visible over lower abdomen. There is no tenderness or rigidity and no palpable masses.

*Laboratory Examinations.*—Wassermann, negative; urinalysis: albumin, 3+; few granular casts; blood chemistry: N.P.N., 55 mg. per cent; sugar, 110 mg. per cent; chlorides, 420 mg. per cent.

Roentgenographic examination following barium meal reveals two round tumors approximately 4 to 5 cm. in diameter, one lying in prepyloric region, and the other in the lower portion of fundus of stomach (Fig. 11). They are freely movable in the stomach and have the appearance of bezoars or two pedunculated benign tumors. There is no six-hour gastric residue. Multiple fluid levels are present in the abdomen.

Subsequent questioning of patient revealed that in the fall several months previously he had eaten large quantities of persimmons.

Wangensteen suction applied and 5 per cent glucose and normal saline solutions administered intravenously. On Dec. 5, 1936, patient passed a hard, round mass about 5 cm. in diameter and black in color. Further examination of this mass confirmed the diagnosis of phytobezoar, probably of persimmon origin.

Following this patient began to improve rapidly and left the hospital in apparently good condition on Dec. 16, 1936.

CASE 7.—J. M., white male, aged 59 years. Admitted to Touro Infirmary March 7, 1937, complaining chiefly of pain in stomach. During dinner one evening in January, 1937, about three months previous to admission, he experienced epigastric discomfort and nausea. Previous to this time he had had no gastrointestinal disturbances. Since then, he has had frequent attacks of nausea and cramplike pain in epigastrium. He is often nauseated but rarely vomits. The pain occurs intermittently throughout the day, is relieved sometimes by eating, but is increased about an hour after eating. The pain seems to be generalized over the entire epigastrium and rarely radiates to any other portion of the abdomen.

*Past History.*—Previously in good health. Patient is a farmer and has persimmon trees in his field. For past three years he has eaten large quantities of persimmons each fall when the fruit ripens. Three years ago when he first began eating persimmons he had some epigastric discomfort and following this for a few days had an attack of diarrhea which he "cured" by drinking oak-bark tea. For a few days following first attack of pain, patient noticed distinct tarry stools, but since then stools have been dark brown in color. Appetite has been good and he has lost very little weight.

*Physical Examination.*—Patient is well developed, well nourished, and not acutely ill. Temperature, pulse, and respiration are normal. There are no significant findings except in the abdomen.

On inspection of the abdomen no abnormality is observed, but on palpation there is felt a rather firm round mass in the epigastrium. It is about 12 cm. in diameter and is freely movable in all directions, but especially up and down. The mass is frequently "lost" during palpation and seems to recede high in the epigastrium and under the left costal margin. There is slight tenderness, particularly on deep pressure, but no rigidity.

*Laboratory Examinations.*—R.B.C. count, 4,880,000; Hb., 80 per cent; W.B.C., 12,000; neutrophils, 70 per cent; small mononuclears, 23 per cent; large mononuclears, 6 per cent; eosinophiles, 1 per cent; gastric analysis: free HCl, 40; total acidity, 60; urinalysis, normal.

Roentgenographic examination after barium meal reveals the barium passing through the esophagus in a normal manner. At the initial swallow of barium, a



large filling defect is seen in the region of the pars media. As the stomach fills, the defect appears to rise toward the fundus of the stomach and the impression gained is that there is a large foreign body within the stomach, either a bezoar or a pedunculated polyp which moves rather freely (Fig. 8). The stomach is very irritable, but at six hours there is a retention of barium, the shadow being very irregular, as though the barium were caught in the meshes of a mass with irregular surfaces. The duodenum appears to be entirely normal and that portion of the meal which has left the stomach is occupying the terminal ileum. At twenty-four hours there are still a number of small flecks of barium in the stomach, apparently adhering to the mass; the remainder is outlining the colon fairly satisfactorily and no lesions are seen.

*Preoperative Diagnosis.*—Diospyrobezoar.

Operation, March 10, 1937: A left rectus incision is made. Upon examination of the greater curvature of the stomach, in the region of the pars media is an area of edema and induration. The adjacent lymph nodes in the gastrocolic omentum are removed for immediate biopsy study. Upon further examination of the stomach, a large mass is found present in the lumen of the stomach which is freely movable and apparently a foreign body. After excluding the peritoneum and exposing only the anterior wall of the stomach, so as to prevent any spillage, an incision is made on the anterior stomach wall in a transverse direction, in order to expose the interior of the stomach. The foreign body, a phytobezoar, is removed. It is oval and measures 14 cm. in length and 9 cm. in diameter. It has a very dark brownish to black color and in some places is smooth as though it was shellacked, while at other places it is rough and pitted. There are nodular bosselations on the outer aspect. The phytobezoar is removed through the opening in the anterior wall of the stomach and an ulcer found on the greater curvature (Fig. 13). The ulcer is round, about  $2\frac{1}{2}$  cm. in diameter, has thickened, over-hanging edges with a dirty granular base (Fig. 12). It is considered that there is no necessity for treating the ulcer, except by removal of the foreign body.

The wound is closed by two rows of suture. The peritoneum is closed in layers with interrupted black silk sutures. The patient made an uneventful recovery.

*Pathologic Report.*—Tissue specimen measuring 3 mm. by 3 mm. by 1 cm. grossly appears to be a small lymph node surrounded by fat. This is confirmed by microscopic examination and there is no evidence of malignancy. The other specimen is a firm, brownish black oval mass measuring 9 by 14 cm., weighing 460 gm. with a pitted, bosselated surface. On section the internal structure has a light brown to yellow color and seems to consist of an amorphous, somewhat friable material with a few skins and persimmon seeds. Upon drying, the mass shrunk considerably in size, weighing about 60 gm., and crumbled readily. This specimen has all the characteristics of a diospyrobezoar.

The patient made an uneventful recovery. He was observed again and stated that he was completely relieved of all complaints. Roentgenologic studies revealed no evidence of the previous ulcer.

CASE 8.—C. H., colored female, aged 44 years. Admitted to Charity Hospital Jan. 7, 1938, complaining of epigastric pain, nausea, and vomiting.

*Present Illness.*—Began in October, 1937, following the ingestion of persimmons. Patient lives on a farm and one evening while walking home after working in the fields all day, she passed a persimmon tree loaded with ripe persimmons. She had not eaten anything since breakfast and was very hungry so she stopped and ate over a dozen persimmons to appease her hunger. Following this she became very thirsty and drank a large amount of water from a near-by well. That evening several hours later she experienced rather severe cramplike epigastric pain followed by marked nausea and vomiting and intense diarrhea. This persisted all through the next day but gradually subsided in a few days. She then felt quite well for a few weeks and

then began having dull pain, constant in character and localized to the epigastrium. Occasionally the pain became quite severe and cramplike. She was conscious of a weight sensation in the epigastrium. The pain seemed to have no relation to meals. Nausea and vomiting have gradually occurred more frequently. She is somewhat constipated. She has not vomited or passed blood by rectum. Appetite is poor and she has lost about ten pounds in weight.

*Physical Examination.*—Patient is somewhat undernourished and not acutely ill. Temperature, pulse, and respiration are normal. Significant findings limited to abdomen, which on palpation reveals a hard mass in the epigastrium just above the umbilicus. It is round and about 7 cm. in diameter. It is freely movable in all directions. There is moderate tenderness but little rigidity.

*Laboratory Examination.*—Wassermann, negative; urinalysis and blood chemistry, normal; R.B.C. count, 4,050,000; Hb., 90 per cent; W.B.C. count, 7,500; neutrophils, 70 per cent; eosinophiles, 3 per cent; small mononuclears, 23 per cent; large mononuclears, 4 per cent.

Roentgenographic report following barium meal fluoroscopically describes extensive filling defect in barium shadow without involvement of stomach wall indicative of the presence of an intragastric foreign body (Fig. 10). At end of six hours there is slight amount of gastric retention. At end of twenty-four hours head of meal has reached descending colon, with partial evacuation at end of forty-eight hours.

A preoperative diagnosis of phytobezoar was made.

Operation, Jan. 22, 1938: Under ether anesthesia left upper paramedian incision is made. Exploration of the stomach reveals a hard mass in the prepyloric region. The stomach containing the mass is delivered into the wound and carefully excluded from the peritoneal cavity by wet cloths. A transverse incision is made in about the middle of the anterior wall of the stomach and a black hard round mass about 6 cm. in diameter and having an irregular surface is removed. Subsequent examination proved this mass to be a phytobezoar, probably of persimmon origin. According to the surgeon's recorded dictation, further exploration of the stomach revealed no other masses. The gastrotomy incision was then closed with three rows of sutures. The abdominal incision was closed in layers.

The patient made an uneventful recovery and was discharged on Feb. 1, 1938, in good condition.

On June 12, 1938, she was readmitted to Charity Hospital complaining of nausea, vomiting, and epigastric pain. She stated that, whereas she remained well for about three weeks after her discharge from the hospital in February, 1938, her symptoms gradually returned and at present her complaints are exactly similar to those she had had on her previous admission. Patient has not eaten any persimmons since discharge from hospital. Abdominal examination revealed a hard, irregular-shaped, freely movable mass about 6 cm. in diameter in the epigastrium. There is slight tenderness but no rigidity.

Roentgenographic examination following barium meal revealed a negative shadow filling the distal end of stomach with displacement of barium suggestive of foreign body, probably a bezoar (Fig. 7). At the end of six hours there was 50 per cent gastric retention and at end of twenty-four hours the meal has reached the descending colon, adherent flecks of barium clearly outline the foreign body in the prepyloric region (Fig. 9).

Operation was performed on June 20, 1938, and a firm pyramidal-shaped mass dark brown to black in color having an irregular surface was removed (Fig. 3). On section it was light brown in color, consisting of an amorphous granular material with a persimmon seed in its center. Subsequent examination proved it to be a phytobezoar, probably of persimmon origin.

The patient had an uneventful recovery and was discharged in good condition on July 4, 1938.

Although the surgeon found only one intragastric foreign body at the first operation, a subsequent examination of the preoperative plate shows the presence of two intragastric foreign bodies, one in the pyloric and the other in the fundic ends of the stomach (Fig. 10). This case illustrates the necessity of careful fluoroscopic, radiographic, and operative examinations in all cases of bezoars.

### SUMMARY

1. A critical analysis of 171 cases of trichobezoars, 119 cases of phytobezoars, and 13 cases of concretions, collected from the world literature, and a presentation of 1 additional case of trichobezoar and 7 additional cases of phytobezoars or persimmon bezoars form the basis of this communication.

2. A succinct historical résumé of bezoars is given.

3. The several varieties of bezoars are classified into trichobezoars, phytobezoars, trichophytobezoars, and concretions. The trichobezoar consists of a large quantity of hair of varying lengths, firmly matted together, frequently completely filling the stomach, and consequently assuming its shape. The phytobezoar is composed of a variety of vegetable material, including fibers, skins, seeds, leaves, roots, and stems of plants molded together and forming a compact mass. The most common form of phytobezoar is due to the ingestion of persimmons. Of the 126 collected cases of phytobezoars, including ours, 92 (73 per cent) were of this type. Because of this fact and because of its distinctive clinical and physical characteristics, it is considered desirable to separate it from other phytobezoars by a more significant term. For this reason we have suggested the term "diospyrobezoar," from the Greek etymon, *Diospyron* (meaning Jove's grain), which is the generic name for the wild persimmon. The most common form of concretion is due to the imbibition by painters or furniture employees of furniture polish, which consists mainly of a strong alcoholic solution of shellac; the drinking of water after its ingestion precipitates the resin into an accumulated mass.

4. Of 142 collected cases of trichobezoars, including ours, in which the age was determined, over 80 per cent occurred *before* the age of 30 years. Of 90 collected cases of phytobezoars, including ours, in which the age was determined, over 70 per cent occurred *after* the age of 30 years.

5. Of 152 collected cases of trichobezoars, including ours, in which the sex was determined, there were 139 (91.4 per cent) females and 13 (8.5 per cent) males. Of 96 collected cases of phytobezoars, including ours, there were 22 (23 per cent) females, and 74 (77 per cent) males.

6. Whereas only 9 per cent of the collected cases of trichobezoars demonstrated some psychic or mental disturbance, trichophagia is considered a "personality maladjustment" and patients exhibiting this

characteristic are believed to have some underlying neurologic or psychiatric disturbance.

7. In discussing the development of phytobezoars, it is necessary to consider them under two groups: (1) diospyrobezoars, resulting from the ingestion of persimmons; and (2) other phytobezoars, due to the ingestion of a variety of other vegetable and plant matter. The mechanism of formation of the former is essentially chemical and depends upon the presence of soluble shibuol, a phlobatannin, which under the influence of gastric juice becomes transformed into a sticky coagulum cementing into a ball pieces of skin and seeds which may be present. On the other hand, the mechanism of formation of other phytobezoars is essentially mechanical and depends upon the insoluble and indigestible fiber content.

8. The characteristic clinical manifestations of trichobezoar are a rather large, firm, freely movable epigastric mass, associated with some pain, nausea and vomiting, anorexia, weakness, and loss of weight. In a series of 131 collected cases of trichobezoars, including ours, an abdominal mass was present in 115 (87.7 per cent); abdominal pain occurred in 92 (70.2 per cent); nausea and vomiting, in 85 (64.9 per cent); weakness and loss of weight, in 50 (38.1 per cent); and constipation and diarrhea, in 42 (32 per cent). Of 94 collected cases of phytobezoars, including ours, these clinical manifestations occurred in 54 (57.4 per cent), 80 (85.1 per cent), 70 (74.4 per cent), 31 (32.9 per cent), and 30 (31.9 per cent), respectively.

9. A slight secondary anemia and a mild leucocytosis are usually observed in cases of bezoars. Gastric analysis in trichobezoars may reveal strands of hair and usually a normal or low acidity. Gastric analysis in phytobezoars usually reveals a normal or hyperacidity.

10. Roentgenographic examination, especially after the ingestion of a barium meal, reveals characteristic findings and almost invariably demonstrates the intragastric nature of these foreign bodies.

11. The prognosis in bezoars depends primarily on the presence or absence of two factors: (1) the institution of adequate therapy and (2) complications. The mortality in the nonoperative collected cases of trichobezoars, diospyrobezoars, and other phytobezoars is 72.7 per cent, 50 per cent, and 66.6 per cent respectively in contrast to the corresponding incidences in the operative cases of 4.8 per cent, 7.4 per cent, and 4.7 per cent respectively. Whereas the mortality in the collected cases of trichobezoars and phytobezoars with complications is 53.1 per cent and 18.7 per cent respectively in those cases without complications, these corresponding figures are 10.4 per cent and 2.1 per cent.

12. The total mortality in the collected cases of trichobezoars, diospyrobezoars, and phytobezoars, including ours, was 19.1 per cent, 9.8 per cent, and 12.5 per cent respectively.

13. The complications resulting from the various types of bezoars are due primarily to: (1) interference with the normal physiologic activity of the gastrointestinal tract; namely, obstruction and exhaustion or inanition; and (2) traumatic irritation to the stomach and bowel wall and its consequences; i.e., mucosal erosion, ulceration, perforation, and peritonitis. Of the collected cases of trichobezoars, intestinal obstruction occurred in 10.8 per cent, gastroduodenal ulceration in 9.6 per cent, perforation of ulcer in 3.2 per cent, peritonitis in 3.8 per cent, and exhaustion in 8.3 per cent. These corresponding incidences in the collected cases of phytobezoars, including ours, were 26.5 per cent, 24.4 per cent, 7.4 per cent, 8.4 per cent, and 1 per cent.

14. Of the collected cases of trichobezoars complicated by peritonitis, perforated ulcer, gastroduodenal ulcer, and intestinal obstruction, the respective mortality incidences were 100 per cent, 100 per cent, 53.3 per cent, and 47 per cent. The corresponding incidences in the collected cases of phytobezoars were 75 per cent, 71.4 per cent, 21.7 per cent, and 16 per cent.

15. The treatment of bezoars and concretions is essentially surgical and consists of the operative removal of the foreign body, usually from the stomach and occasionally from the intestines.

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# SURGERY

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## Original Communications

### POLYPOID DISEASE OF THE COLON

#### A PROPOSED SURGICAL PROCEDURE IN SELECTED CASES

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IN RECENT years the literature on polyps of the colon has become extensive. Interest has been stimulated in this rather rare disease because of the increasing frequency with which the lesions are found, due to modern methods of examining the colon. Also, the striking tendency of these tumors to undergo malignant changes has been the basis of interest in many of the pathologic reports. However, comparatively little has been learned and the knowledge of this disease remains much as it was in 1916 when Murphy<sup>50</sup> said: "The etiology of intestinal polypi—like the common wart—is shrouded in mystery; whence they come, why they go, is like the riddle of the Sphinx."

#### TERMS

Much confusion appears in the literature regarding the terminology of polyps of the colon.<sup>68</sup> Terms appear such as polyposis, multiple polyposis,<sup>2, 47, 66</sup> multiple adenomas,<sup>27, 34, 59, 61</sup> polyposis intestini,<sup>65</sup> polypoidosis,<sup>6</sup> polypoid disease, disseminated polyposis.<sup>70</sup> Hence, it is often difficult to ascertain the type of pathology under discussion. The term used by one writer in describing polyps, limited to an anatomic segment, may be used by another in describing a colon entirely lined with polyps. Also, pathologic terms are freely intermingled with clinical terms which adds to the difficulty.

A polyp is a growth from a mucous membrane, either pedunculated or sessile, made up of hypertrophied mucous membrane, or it may be a true tumor. When there is more than one, they are, of course, multiple. Hence, multiple polyps may mean two polyps located in the colon or thousands of polyps studding the entire large bowel. Bnie<sup>6</sup> has clarified

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connective tissue. Hence, the growth is downward, extending into the muscularis mucosa. This type is the most malignant.

Duke<sup>24</sup> believes that the pedunculated types are not as dangerous as the sessile types, but that on the cap of pedunculated polyps malignant changes may occur. He points out that in the sessile variety the pathologic characteristics are the branching of the villi, the bowing upward of the muscularis mucosa with the formation of a catarrhal collar around the periphery, and in the clefts between the primary and secondary tumors. These cells, he states, are the ones that undergo malignancy.

#### RELATIONSHIP TO MALIGNANCY

Nowhere, according to Ewing,<sup>26</sup> can be demonstrated more clearly the logical transition from simple inflammatory hyperplasia to tumors which are morphologically, pathologically, and clinically adenomas and carcinomas.

Coffey (quoted by Graham<sup>34</sup>) says: "There is probably no benign process in which there is a higher incidence of malignancy than colonic polyposis." Lockhart-Mummery states: "Almost all recorded cases of multiple polypi of the colon eventually become malignant."

Hullsick,<sup>38</sup> in an analysis of 127 cases of multiple polyposis, found the incidence of carcinoma to be 36.4 per cent. Soper,<sup>64</sup> in 61 cases, discovered malignancy in 26, or 43 per cent. In a study of 166 colons containing polyps, Lawrence<sup>42</sup> found 19 cases, or 11.4 per cent, to have existing malignancy.

Many<sup>54, 65</sup> believe that most carcinomas of the colon have their origin in polyps. Rankin<sup>56</sup> says: "I believe that it is a reasonable conclusion that a great many carcinomas of the colon, perhaps more than we suspect, are thus etiologically explainable. The commonest sites of polyps and carcinoma of the lower end of the gastrointestinal tract are the sigmoid and rectum. The ratio of eight cancers of the sigmoid and rectum to one in the rest of the colon is maintained in the incidence of polyps."

#### ETIOLOGY

Although a great deal of study has been given to this disease, the etiology remains obscure. In the acquired type the polypoid formation (pseudopolyposis)<sup>73</sup> is, undoubtedly, a hyperplastic response to inflammation. Polypoid growths in the colon, secondary to ulcerative colitis, are relatively common. Bargen and Comfort<sup>4</sup> found 69 such cases in 693 patients suffering from ulcerative colitis. They state that "of five cases of multiple polyposis, four will be on the basis of ulcerative colitis." Amebiasis,<sup>1</sup> bacillary dysentery, and other infections<sup>41, 62</sup> of the colon have also been reported as the primary causes of these growths.

The etiology of the adolescent (congenital) type has been the basis of much interest. The tendency of this disease to occur in families was rec-



the nomenclature of this disease by calling any condition in which two or more polyps are present in the colon multiple polypoid disease. To this term he appends the segment of colon involved to describe the condition. Thus, when only the sigmoid contains polyps, the condition is known as multiple polypoid disease of the sigmoid. When the entire colon is lined with polyps, it is known as multiple polypoid disease of the entire colon. The use of these terms is clear and simple and they will be used throughout this paper.

#### CLASSIFICATION

Polyps of the colon include any tumor which projects into the lumen of the bowel. Any of the tissue elements forming the component parts of the bowel wall are capable of such growths. Hence, hemangiomas, fibromas, lipomas, myomas, and adenomas may be considered under the term polyp. However, only the adenomas, which are more numerous than all of the other varieties combined, offer exceptional interest to the surgeon and pathologist.

Erdmann and Morris<sup>25</sup> have classified these tumors into: (1) adult (acquired) type, (2) adolescent (congenital, disseminated) type. This classification, although used most frequently in the literature, is of limited value in many cases. By this grouping polyps develop after birth (acquired type), or there is a factor present prior to birth which predisposes to the formation of polyps (congenital type). This classification leaves much to be desired when one attempts to study the origin, age incidence, segmental distribution, and necropsy findings in this disease of the colon.

Bargen and Comfort<sup>4</sup> classified multiple polyps from the standpoint of origin as follows: (1) preexisting inflammatory disease (colitis), (2) arising as innumerable polypoid projections without inflammation, (3) few disseminated adenomatous growths discovered at autopsy.

Excellent histologic studies of polyps of the colon have been made by Schmieden and Westhues,<sup>63</sup> Fitzgibbon,<sup>30, 31</sup> David,<sup>15</sup> Dukes,<sup>24</sup> and others. The conclusions of Schmieden and Westhues are similar to Fitzgibbon's. They classify polyps into three groups. In Group I the polyps are usually solitary and long, covered with normal epithelium. The stalk is made up of loose connective tissue. There is no branching of the villi. These polyps are benign. In Group II there are changes in both the epithelium and connective tissue. The epithelium has bulk and the cells are compressed from side-to-side, producing multilayered buds. The nuclei are elongated and take a deep stain. The villi are branched and there are papilla-like projections into the lumina of the glands. These polyps are potentially malignant. In Group III the structural changes are more exaggerated than in Group II. There is great proliferation of the epithelium. The arrangement of the cells is distinctly irregular. This proliferation is out of proportion to the growth of the underlying

## AGE

Multiple polypoid disease of the entire colon is said to be most common between the ages of 15 to 35 years. Hullsiek<sup>39</sup> found the average age to be 30.9 years in the 127 cases he reviewed from the literature. Doering,<sup>22</sup> in an analysis of 52 cases, also believes that this age group is the most commonly affected. In his analysis he found the youngest to be 5 years and the oldest 62. McKenney<sup>47</sup> reported a case in a child 2 years of age.

Polyps incidentally discovered in routine autopsies were found to be more numerous in older individuals. Lawrence<sup>42</sup> after studying 166 colons with multiple polypoid disease found 87.4 per cent to be over 40 years of age. Lawrence's figures differ from those of Hullsiek and Doering because he undoubtedly is speaking of multiple polypoid disease while they refer to multiple polypoid disease of the entire colon. The variance in these figures might infer that the two conditions are different clinical entities.

## SEX

Most investigators agree that multiple polypoid disease of the entire colon is more common in males than females. In segmental multiple polypoid disease the incidence is about equally distributed.

## NUMBER OF POLYPS AND SEGMENTAL DISTRIBUTION

The distal colon and rectum are involved most frequently. Soper found the rectum to be involved with polyps in 95 per cent of 61 cases. Thorbeeke<sup>69</sup> also discovered this to be true in 80 per cent of his cases. He found that in 31 out of 54 cases in which rectal polyps were discovered there also existed polyps higher in the colon.

Lawrence<sup>42</sup> found that in all but 64 of 166 cases the distribution was restricted to a particular site. The distribution in his cases is shown in Table I:

TABLE I  
POLYPS OF THE COLON (IN 166 CASES) IN 7,000 AUTOPSIES

	NO.	PER CENT
Cecum	46	16.1
Ascending	48	16.7
Hepatic	18	6.3
Transverse	48	16.7
Splenic	23	8.0
Descending	48	16.7
Sigmoid	56	19.5
	287	100.0

The number of polyps found in the 166 cases is as follows:

Single polyps	71
Double polyps	28
Triple polyps	27
Many polyps	37
Throughout colon	13

ognized by Cripps<sup>14</sup> in 1882. Since then many familial cases have been reported.<sup>36, 40, 52, 72</sup> Hullsiek<sup>37</sup> obtained a positive family history in 11 per cent of 127 cases. Dukes,<sup>23</sup> Lockhart-Mummery, McKenney,<sup>47</sup> and others have experienced the difficulties and the tremendous tasks involved in rounding up the members of families to ascertain the frequency of polyps. Lockhart-Mummery<sup>43</sup> believes that the disease is transmitted as a Mendelian dominant. He says that "a change, or mutation, has taken place in the genes of some individual who has not personally exhibited the diseased condition, but who has passed the mutated genes on to his descendants."

The most striking tendencies of this disease to occur in families have been in cases reported in which the entire colon contained polyps. This familial tendency is not so definite in cases where only a segment of colon is involved. Buie, in this connection, states: "It is possible to be almost definite in the statement that usually only those instances in which the entire colon is involved by polypoid disease fit into the heredo-familial classification." Stewart<sup>65</sup> also agrees when discussing polyposis intestini (entire colon involved) that "this would appear to be merely an extreme grade of the condition of multiple polypi (segmental) already mentioned, were it not that there is a constitutional hereditary factor non-existent in the more banal variety."

The term heredofamilial tendency in this disease implies that the epithelial covering in the colon possesses some factor which predisposes it to tumor formation. In other words, there is present a mucosa which may have a "lowered threshold to stimuli," or else the inhibitive powers governing regulated growth are lost.<sup>60</sup> When these inherent factors exist, stimuli, which are normally present, are often sufficient to produce a proliferative response.

From an experimental point of view, very little has been done on the production of polyps in laboratory animals. Hoelzel and Da Costa<sup>35</sup> claimed to have produced polyps in the colons of rats by feeding them inert material, such as kaolin, barium, and talcum. This work, however, has not been repeated with similar results.<sup>44</sup>

#### INCIDENCE

Although multiple polypoid disease is usually considered a rarity, such might not be the case if routine examinations of the rectum and colon were done. Buie reports that at the Mayo Clinic between 1925-1935 there were 1,234 patients with polypoid disease. One of every 35 patients who complained of a disturbed function of the colon presented this condition.

Lawrence<sup>42</sup> found 166 cases of polypoid disease in 7,000 autopsies at Cook County Hospital (2.37 per cent).

Feyerter<sup>29</sup> examined 1,800 consecutive colons at autopsy and found polyps in 386 cases (21.4 per cent).

been unsuccessful. Astringent drugs, such as quinine, tannic acid, and magnesium chloride, have been used in the form of colonic irrigations without results.

Deep x-ray therapy has been employed by Barker,<sup>3</sup> McKenney,<sup>47</sup> and others.<sup>1, 11</sup> Its use has been attended by the passage of grapelike, neerotic growths found in the stool with an improvement of symptoms. However, no case has been reported in which all of the polyps have disappeared following this therapy.

Fulguration of all polyps within the reach of the sigmoidoscope should be carried out without delay. To one experienced in the use of the sigmoidoscope, polyps may be fulgurated above the rectosigmoid. The danger of fulgurating too extensively, with resulting perforation, should always be kept in mind.

Various surgical procedures have been advocated.<sup>7, 12, 21</sup> Divergence of the fecal current by the use of ileostomy and colostomy occasionally has been followed by the disappearance of the tumors in the portion of the bowel put to rest.<sup>33</sup> Isolated polyps may be excised<sup>55</sup> or the segment of the bowel embracing these tumors may be resected.<sup>10, 19, 20, 51</sup>

When multiple polypoid disease of the entire colon is present, total colectomy<sup>40, 55, 56</sup> offers the only hope for those unfortunate individuals affected. An ileostomy is done when the entire colon and rectum are resected. If the rectum and lower sigmoid are preserved, an ileosigmoidostomy<sup>18</sup> is done prior to resection of the remaining colon. In this procedure all existing polyps of the rectum and remaining sigmoid are removed by fulguration from below.

Mayo and Wakefield<sup>46</sup> have reported a procedure used in dealing with multiple polypoid disease of the entire colon in which an ileosigmoidostomy and colectomy were done. The distal sigmoid was brought out as a colostomy. Through this opening all polyps which could not be reached from below were fulgurated. Later the colostomy was closed. Fansler,<sup>28</sup> in discussing this operation, cited a case in which he had fulgurated polyps through a colostomy. He also mentions the potentialities of such a procedure.

As it was stated above, all therapeutic measures should be aimed at the early eradication of the tumor tissue. In many cases the polyps may be few in number and limited to a segment of the colon.<sup>45</sup> Also, cases may be encountered in which a few polyps are distributed in more than one segment of the large bowel. These conditions are often seen in young individuals who are otherwise healthy. To recommend a radical procedure, such as a colectomy, imposes on the surgeon a great responsibility and on the patient a great danger. In many of the cases most of the colon is normal from a clinical standpoint. And who, in our present state of knowledge of this disease, is in a position to say that the entire

Stewart<sup>65</sup> found the following in 127 cases:

Single polyps	70
Several polyps	43
Large number	14

From the above it will be seen that multiple polypoid disease of the entire colon is relatively rare compared with the number of cases in which a single polyp is present or in which the distribution of polypoid disease is limited to a segment of the colon.

#### SYMPTOMS

The symptoms in this disease vary to a great extent with the location and extent of the pathology present. Quite frequently the entire colon has been involved with only a minimum of symptoms and with little discomfort to the patient. However, changes in bowel habit are usually the first noted. This may vary from an occasional soft stool to a profound diarrhea. Accompanying these changes, blood and mucus are often discovered in the stool. The loss of blood may be sufficient to produce a marked anemia. Indefinite abdominal pain<sup>13</sup> is often present, although the pain is usually located over the site of pathology.<sup>67</sup> At times, intermittent, crampy, colicky pain may be the first symptom. This is often indicative of a partial intussusception<sup>9</sup> caused by violent peristaltic contractions. Audible abdominal noises may be noticed. Tenesmus is most frequent when polyps are located in the distal colon and rectum.

#### DIAGNOSIS

A carefully taken history, together with an examination of the rectum and distal colon, is usually sufficient to suggest the diagnosis. The stool should be submitted to a thorough examination to determine the presence of amoebae or other parasites. Suffice it to say that all patients should be given the benefits of a careful proctoscopic examination. When properly done, the lower 20 cm. of the bowel can be examined without discomfort to the patient. When polyps are found, the entire colon should be submitted to a roentgenologic examination to ascertain the presence of polyps higher in the colon. To accomplish this the double contrast method is employed. The painting of the bowel wall after it has been distended with air and the visualization by stercoroentgenographs, as advocated by Weber,<sup>71</sup> serve as the best available means of investigating the colon. An expert roentgenologist, by using this method, can visualize polyps less than 1 cm. in diameter.

#### TREATMENT

Until the etiology of polypoid disease is better understood, all therapeutic measures must be directed at the eradication of the tumor tissue. Dietary measures aimed at the reduction of roughage in the diet have

Hospital. Buie sigmoidoscopes of various lengths were introduced through the colostomy openings to determine the possibility of visualizing the interior of the large bowel. It was found, by careful manipulation of the scopes, that the interior of almost the entire colon could be visualized. This was accomplished despite the fact that the colostomy openings were often small due to the contraction of the surrounding structures. Had the colostomy been made with the idea in mind of passing a sigmoidoscope, the visualization of the interior of the bowel would have been greatly facilitated. X-ray pictures have been taken with the sigmoidoscope inserted through a colostomy in the left colon (Fig. 1).

Inflated descending colon.

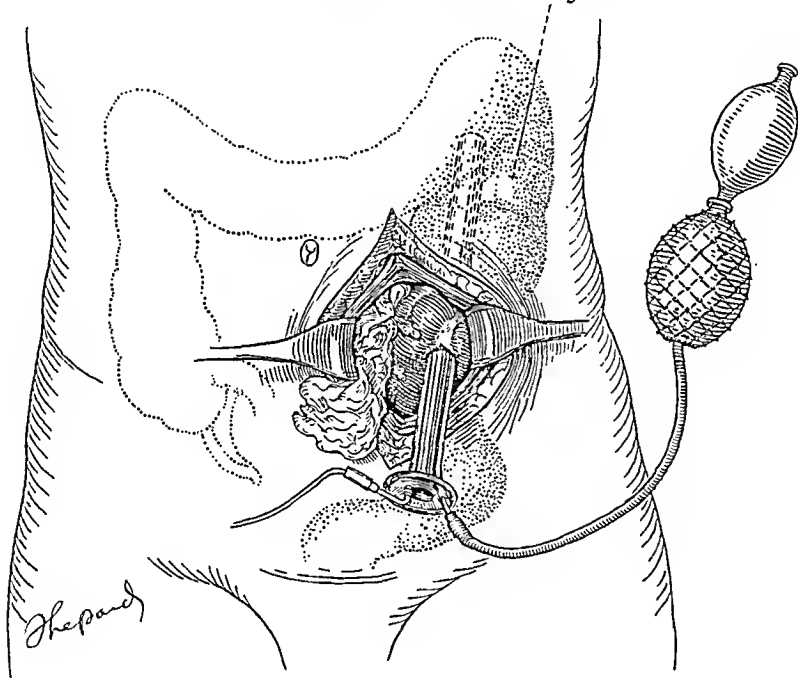


Fig. 2.—Diagrammatic drawing showing the introduction of the scope at the time of one-stage operation.

The success with which the interior of the bowel could be seen strongly suggests that polyps in the colon could easily be fulgurated by this method.

The procedure could be carried out in one stage or two stages (Figs. 2-4). It is proposed that if polyps are present in the left colon they could be fulgurated through a colostomy in the left colon (Fig. 4). A colostomy in continuity<sup>17, 32</sup> would obviate the necessity of crushing a spur when fulguration of the tumors was completed. The colostomy could be closed over and the colon replaced into the peritoneal cavity.<sup>16</sup> Protective walling off of the peritoneal cavity<sup>53, 57</sup> would safeguard against peritonitis from the exteriorized bowel.

colon should be sacrificed? In this connection one is confronted with many perplexing questions. How long have the polyps been present? Is a colon, in which only a segment is involved, destined in time to become studded with polyps? Or will malignancy and death occur before sufficient time has elapsed for the disease to involve the entire colon? Is segmental polypoid disease a different pathologic entity from multiple polypoid disease of the entire colon? Is the heredofamilial factor present to the same degree in both types? Does malignant degeneration occur equally in both types? If this is so, why are polyps discovered so frequently at autopsy in the aged? Are polyps found late in life all on an inflammatory basis or have they been present since birth? Could all



A.

B.

Fig. 1.—A, Sigmoidoscope entering a left colostomy and passing into sigmoid colon; B, sigmoidoscope entering a left colostomy and passing into the splenic flexure.

polyps of the colon be caused by an organism which so far has not been isolated? These questions in our present state of knowledge cannot be accurately answered.

#### PROPOSED SURGICAL PROCEDURE

When a segment of the colon is involved with polypoid disease or when only a relatively few polyps are present throughout the colon, it would seem rational that an attempt should be made to remove successfully the tumors without sacrificing the entire colon. Fulguration of the tumors through a properly placed colostomy appears to be the only possible method by which this objective could be attained. With this thought in mind, several patients with colostomies were studied at Cook County

In a like manner, polyps located in the hepatic and splenic flexures, as well as the transverse colon, could be fulgurated through a transverse colostomy (Fig. 3). A cecostomy<sup>48</sup> would serve as the best site for the introduction of the sigmoidoscope to fulgurate polyps located in the cecum and ascending colon (Fig. 4).

Exteriorizing the colon, thereby making a two-stage procedure, permits painstaking fulguration and observation of the healing areas. Should it be found that a portion of the tumor had been inadvertently missed, subsequent fulguration is possible by this two-stage procedure.

Fulguration of polyps could also be done in a one-stage operation (Fig. 2). By carefully walling off the field to prevent contamination, an opening could be made along the anterior longitudinal band, large enough to admit the sigmoidoscope. The assistant surgeon could be helpful in manipulating the scope from the peritoneal side of the bowel. In this way fulguration would be facilitated and the sites could be inspected for possible perforation. Following the thorough fulguration of all polyps in the segment, the opening in the wall of the colon could be closed in the usual manner.

The advantages of the one-stage procedure are that the patient has but one operation and does not have to tolerate a colostomy (Fig. 2). The fulguration in this operation must be complete because there is not another opportunity for inspection and subsequent fulguration. The chances of peritoneal soiling are greatly increased in the one-stage procedure.

The danger of perforation of the bowel wall, as a result of fulguration, is always present. However, it is certainly no greater than when polyps located in the sigmoid, above the peritoneal reflexion, are fulgurated through a scope passed from below.

When one is confronted with a patient with multiple polypoid disease of the entire colon, in whom a radical procedure, such as a colectomy, is contraindicated, the method proposed may be of some value. By painstaking fulguration through multiple colostomies, large numbers of polyps could be removed, thus decreasing the malignant potentialities of the disease.

#### SUMMARY AND CONCLUSIONS

1. The terminology and classifications used in the literature regarding polypoid lesions in the colon are confusing.
2. There is definite evidence that polypoid lesions of the colon undergo malignant changes.
3. The etiology of this disease is not understood. It appears that multiple polypoid disease limited to a segment of colon differs etiologically and pathologically from multiple polypoid disease of the entire colon.



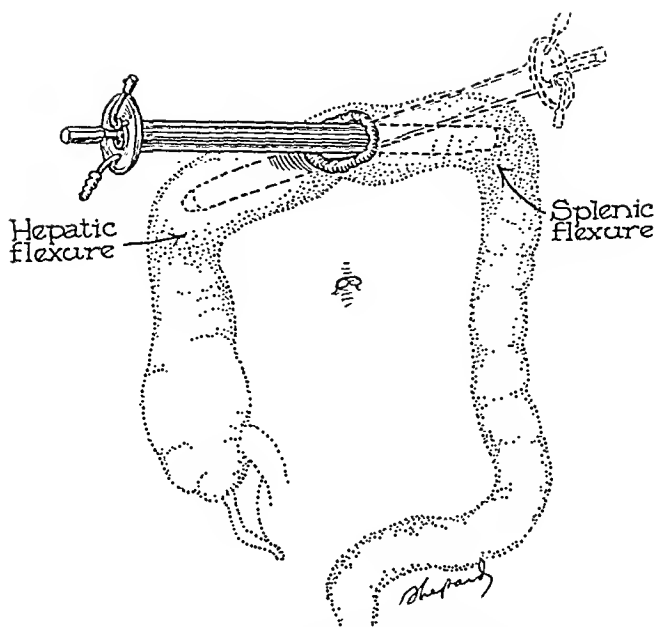


Fig. 3.—Diagrammatic drawing showing scopes entering a transverse colostomy. Polyps located in the transverse colon, hepatic or splenic flexures could be fulgured by this proposed two-stage procedure.

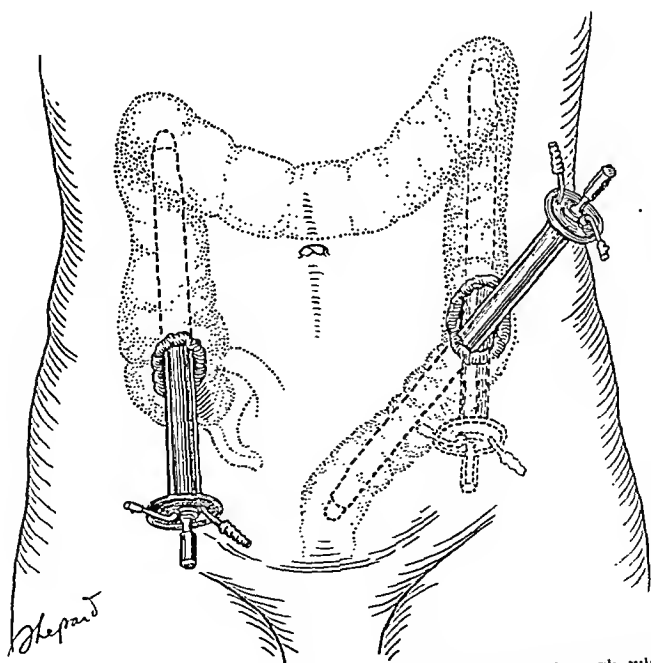


Fig. 4.—Diagrammatic drawing showing location of colostomies through which polyps in the right and left colon could be fulgured; two-stage procedure.

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2. There is definite evidence that polypoid lesions of the colon undergo malignant changes.
3. The etiology of this disease is not understood. It appears that multiple polypoid disease limited to a segment of colon differs etiologically and pathologically from multiple polypoid disease of the entire colon.

4. Sigmoidoscopic examinations and double contrast stereoroentgenographs establish the diagnosis of this disease.
5. The various types of treatment are outlined.
6. It is proposed that polypoid lesions in the colon could be fulgurated through properly placed colostomies.

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# GRADUAL COMPLETE OCCLUSION OF THE CELIAC AXIS, THE SUPERIOR AND INFERIOR MESENTERIC ARTERIES, WITH SURVIVAL OF ANIMALS: EFFECTS OF ISCHEMIA ON BLOOD PRESSURE

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**R**ENEWED interest in ischemia as a factor in the causation of hypertension has been stimulated by the work of Goldblatt and his associates.<sup>1</sup> They found that a persistent elevation of the systolic blood pressure may be associated with the renal ischemia that is produced by partially occluding the renal arteries.

Longeope and McClintock<sup>2</sup> in 1910 determined the effects on the blood pressure of dogs of constriction of the celiac axis and superior mesenteric artery by means of aluminum bands. They found that neither cardiac hypertrophy nor hypertension followed the narrowing of the mouths of these vessels. Autopsies several months following the operations showed no abnormalities except perhaps some congestion of the liver. In none of the animals were both the celiac axis and superior mesenteric artery completely occluded. Jansen, Tams, and Achelis,<sup>3</sup> in acute experiments, found that the rise in pressure resulting from constricting the splanchnic vessels was increased by additional obstruction of the vessels of an extremity.

The abdominal organs, excepting the kidneys and adrenals, are supplied arterial blood in the main by the celiac axis and the superior and inferior mesenteric arteries. If all of these vessels are occluded at one time, death results. The purpose of the present studies was to determine whether or not dogs will tolerate complete occlusion of these vessels in stages and, if so, what the effect on the arterial blood pressure would be. In additional experiments the effects on the blood pressure of occlusion of the main arteries of the extremities and of the head were studied.

## METHODS

Dogs were used in all studies. The blood pressure in all instances was determined by puncturing the femoral artery with a needle which was connected to a mercury manometer. The value obtained is approximately the mean blood pressure. All of the operations were performed under ether anesthesia. The celiac axis and the superior mesenteric

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artery were approached through an incision in the left flank and the inferior mesenteric artery was exposed through a low abdominal incision. Although there was some variation, the usual order of operations was as follows: At the first operation, the celiac axis and superior mesenteric artery were exposed near the aorta and were constricted by Goldblatt clamps.\* After several weeks, the interval depending upon the condition of the animal, this constriction was increased. Several weeks subsequently, the inferior mesenteric artery was doubly ligated and divided. Approximately one month subsequently, constriction of the celiac axis and the superior mesenteric artery was made complete. The arterial blood pressure was determined frequently.

#### RESULTS

A total of twenty-nine animals was used in this study. Fourteen of these died at varying times following the first operation. A large proportion of these deaths occurred in the earlier experiments and were due almost certainly to too great constriction of the celiac axis and superior mesenteric artery. A number of these passed stools containing blood. Five of the animals died following the second operation, two after the third, and one following the fourth. The last operation on the latter animal had been performed sixteen days previously. The body weight of most of them declined markedly. The remaining seven animals survived complete occlusion of the three main vessels and apparently remained in good health. There was some loss in weight during the process of occluding the vessels, but this was regained subsequently.

Since the alterations in blood pressure were not great, they will not be recorded in detail. None of the animals exhibited a marked increase in the pressure. Unless the animal became quite ill following the operation, there was usually a rise in blood pressure of approximately 20 mm. Hg. which tended to return to the control level after a few days. Subsequent additional constriction was usually associated with a slight elevation in pressure. Two animals showed a persistent elevation of approximately 15 mm. during the two months periods that the pressure was followed after having caused complete constriction of the three main vessels. Palpation of the arteries of the mesentery of the intestine failed to reveal pulsation in two of the three instances in which this region was explored after the three main vessels had been occluded. Despite the absence of a palpable pulsation, the animals ate heartily and appeared to be well.

Antopsies were performed on three of the animals in which the three vessels had been completely constricted. The vessels were found to be entirely occluded by an organized clot. The Goldblatt clamps had cut through and were lying in a pocket of fibrous tissue. The occlusion had been complete for at least six months in one of these animals. No gross

\*Furnished through the courtesy of Dr. Harry Goldblatt, Cleveland, Ohio.

abnormalities of the abdominal viscera were observed. The lumbar arteries were believed to be somewhat enlarged. No attempt was made to determine the collateral pathways by which the blood reached the organs normally supplied in the main by the three large vessels.

Five animals with complete occlusion of the three vessels are alive at present and are being used in other studies in which additional vessels are constricted. The period of complete occlusion of the celiac axis, the superior and inferior mesenteric arteries in these animals varies from three to nine months. They appear to be entirely normal.

In addition to the studies which have been enumerated, the effects of occlusion of other large arteries on the systemic blood pressure have been determined. The first of these consisted of gradual occlusion of the main arteries to the liver by a procedure similar to that described recently by Huggins and Post.<sup>4</sup> When the occlusion was produced gradually, the animals remained in good condition. No elevation in the arterial blood pressure was observed in the two animals which were studied. The second group consisted of seven experiments in which the two common iliaes and the two subclavian arteries were doubly ligated and divided. The blood pressure in these studies was determined in the carotid artery which was placed beneath the skin of the neck. Several of the animals showed a temporary rise in pressure of about 10 mm., but this was not sustained. The third group consisted of five experiments in which the two common carotid arteries and the two vertebrals were doubly ligated and divided. This was usually done in two stages, one carotid and both vertebrals being occluded at the first operation. Four of the five animals showed for a few days a temporary rise in pressure ranging from 10 to 60 mm. Both vertebrals and both carotids were ligated at one time in the experiment in which the greatest rise in pressure was encountered. The pressure remained definitely elevated for more than two weeks in this animal.

#### DISCUSSION

The main objects of the present study were to determine: first, whether or not dogs will survive gradual permanent occlusion of the main vessels to the intestinal tract and associated organs; and second, the effect of these procedures on the blood pressure. It was rather a surprise to us that a good many of the animals remained in remarkably good condition after the three main vessels had been occluded. It is likely that the percentage of survivals would have been greater if the degree of constriction had been smaller at the onset and if the time interval between operations had been lengthened. As has been stated, a large proportion of the dogs lost a great deal of weight. It seems likely that this was due either to the repeated operative procedures or to the effect of intestinal ischemia on the digestive functions. These points should be investigated further. The observation that animals may re-



main in good condition without pulsations in the arteries to the intestinal tract should be confirmed.

As stated, Goldblatt and his associates<sup>1</sup> found that hypertension may be produced by causing renal ischemia. They found that partial occlusion of the splenic and femoral arteries did not result in hypertension. We have found that a permanent elevation in the systemic blood pressure is not associated with occlusion of the main arteries of the extremities, of the head, of the liver, or of the intestinal tract, including the spleen, pancreas and liver. The results indicate that ischemia of the kidneys is necessary for the production of this type of hypertension. Although no definite conclusions can be drawn, the results substantiate the rather generally accepted view that arteriosclerosis of the large arteries, excepting the renals, is not a frequent cause of hypertension. Apparently the narrowing of the vessels is soon compensated for by collateral anastomoses. Longcope and McClintock<sup>2</sup> studied on autopsy specimens the relationship between sclerosis of the branches of the abdominal aorta and the weight of the heart. They state: "Indeed, of the twenty-one cases in which the splanchnic vessels were narrowed, only seven were associated with any degree of cardiac hypertrophy and in all seven cases a definite chronic nephritis coexisted."

The effect of renal ischemia in animals in which large vessels elsewhere have been occluded previously is being investigated.

#### SUMMARY

Gradual complete occlusion of the celiac axis and the superior and inferior mesenteric arteries may be produced in dogs without causing death or a permanent impairment in health. A sustained elevation in the systemic blood pressure was not encountered in these experiments. Neither is a permanent elevation in pressure associated with occlusion of the main arteries to the extremities or head.

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## EFFECT OF PARTIAL GASTRECTOMY ON ACIDITY AND PEPTIC ACTIVITY OF GASTRIC JUICE

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AN OPPORTUNITY of studying certain problems in the control of gastric secretion has been afforded by follow-up observations on patients with partial gastrectomy. The fact that this operation recently has been more widely advocated in the surgical treatment of selected cases of peptic ulcer suggests the importance of understanding the physiologic principles underlying the successful application of this procedure.

It is generally believed that the antral portion of the stomach controls the chemical or so-called second phase of gastric secretion and that removal of the antrum results in a decrease in the amount of acid and pepsin secreted.<sup>1</sup> Studies in the dog have shown that free hydrochloric acid is usually not present in the gastric contents after partial gastrectomy. By means of a Pavlov pouch, however, it may be demonstrated that the stomach still retains some capacity to secrete hydrochloric acid even after complete removal of the antrum. It is believed that this secretion is usually neutralized in the main stomach by regurgitated intestinal juices and anacidity results.

There is a considerable difference of opinion concerning the effect of partial gastrectomy on gastric acidity in man. The proportion of cases in which achlorhydria has been demonstrated varies widely and there is disagreement regarding the interpretations of the findings. If, however, the reported results are classified according to the technique of gastric analysis employed, these variations appear to be clarified (Table I).

When a single aspiration of stomach contents is carried out approximately one hour after a test meal, no free acid is found in the majority of cases.<sup>2-4</sup> If aspirations are performed at repeated intervals after a test meal, free acid is more frequently demonstrable,<sup>5</sup> and if a technique of continuous suction be employed<sup>6</sup> free hydrochloric acid can be shown to be present in most instances. Free hydrochloric acid also may be found in a higher proportion of cases if histamine is used as a stimulus to secretion.<sup>7-9</sup>

TABLE I

INCIDENCE OF ACHLORHYDRIA AFTER PARTIAL GASTRECTOMY FOUND WITH DIFFERENT METHODS OF GASTRIC ANALYSIS\*

INVESTIGATOR	METHOD OF GASTRIC ANALYSIS	NUMBER OF CASES EXAMINED	PERCENTAGE OF CASES WITH ACHLORHYDRIA
Lorenz and Schur, 1922	Simple test meal	55	75%
Smidt, 1924	Simple test meal	100	79%
Lewisohn, 1923	Simple test meal	10	60%
Strauss et al., 1937	Histamine or test meal	31	58%
Gorvett and Talbot, 1937	Fractional test and histamine	26	65%
Neumann, 1932	Fractional alcohol meal	44	57%
Klein, 1935	Fractional gruel meal	35	32%†
Comfort and Osterberg, 1931	Histamine and continuous aspiration	?	20%
Neeheles and Scheman, 1934	Continuous suction	20	10%

\*Most of the groups enumerated in this table include several types of gastric resection.

†Klein found a higher incidence of achlorhydria six months after operation.

Although differences of technique appear to offer at least a partial explanation of the discrepant results obtained by different investigators, other factors may play a role. In any series of patients subjected to partial gastrectomy, the size of the resected portion of the stomach varies considerably. It has been stated that those patients in whom the antral portion of the stomach has not been completely removed continue to show free hydrochloric acid.<sup>2, 3</sup> Others have maintained that anacidity develops slowly after operation and that the incidence of achlorhydria depends upon the postoperative time interval.<sup>5</sup> The site of the original ulcer has also been thought to be influential in determining the effects of this operation upon gastric secretion, anacidity being found more frequently by some workers after resection for gastric ulcer.

A few studies of gastric pepsin after partial gastrectomy have been carried out. Lorenz and Schur,<sup>2</sup> using the Mett tube method reported that the peptic activity of gastric juice is sometimes diminished after operation but frequently remains within normal limits. More recently, Neumann<sup>10</sup> has reported that pepsin is either absent or is present in only traces in those patients with anacidity after operation. The modern and more precise techniques for peptic determination have not been used.

In the present study we have analyzed the gastric secretion of a series of patients after partial gastrectomy for peptic ulcer in an attempt to clarify some of the above problems. It was also hoped that this study might yield an explanation for the success or failure of the operation in the treatment of ulcer.

Twenty-six patients upon whom partial gastric resection had been performed for peptic ulcer were selected at random from the Surgical Follow-up Clinic of the Presbyterian Hospital. Eleven patients had

originally suffered from gastric ulcer; 13, from duodenal ulcer; and 2, from combined ulcers. An anterior or posterior Polya operation had been performed in 19 cases and the Billroth II operation in 7 cases. Anteoperative gastric analyses, secured in 13 cases, had shown the presence of free hydrochloric acid. The interval which had elapsed between the operation and the time of examination varied from one month to nineteen years.

The gastric contents were obtained by single aspiration one hour after an Ewald test meal. After filtration of the gastric juice, the free and combined acidities were determined by titration with sodium hydroxide. Pepsin determinations were carried out by the hemoglobin digestion method of Anson and Mirsky.<sup>11, 12</sup> For the sake of simplicity, results are expressed in milligrams of pepsin U.S.P. 1:4,000. Hydrogen ion concentration determinations were done colorimetrically. No attempt was made to obtain or to estimate the total volume of gastric contents but in most instances the quantity of gastric juice obtained by aspiration was small.

*Gastric Acidity (Table II).*—Free hydrochloric acid was absent in 22 cases, diminished in 3 cases, and within normal limits in 1 case. Combined acidity exceeded 10 degrees in 16 of the 26 cases and was as high as 24 degrees in 1 patient with achlorhydria. The pH of the gastric contents not containing free hydrochloric acid varied between 4.2 and 6.4 and was in the neighborhood of 5.0 in the majority of instances. The pH of the specimens containing free acid was approximately 1.2 to 1.4.

In analyzing these results, no explanation could be found for the failure of four of our patients to develop anacidity. There was no relation between the postoperative time interval and the presence of free acid or the amount of combined acid. Achlorhydria was usually manifested both in recently operated cases and in patients operated upon from five to fifteen years previously. There was no tendency for free acidity to persist in patients who had originally suffered from ulcer of the duodenum, as was suggested by Klein.<sup>4</sup>

Two of the four patients (Cases 20 and 26) whose gastric secretion still contained free hydrochloric acid had had very extensive gastric resections. It was impossible to determine in retrospect the amount of stomach which had been removed at operation in many instances. The impression was gained, however, that the antral portion of the stomach had not been completely removed in some of our patients with anacidity.

*Intestinal Regurgitation (Table II).*—The presence of regurgitated intestinal juice in the gastric contents was indicated by a yellow or green color in all but two of our patients. One of the remaining two colorless specimens contained free hydrochloric acid.

*Peptic Activity (Table II).*—Determinations of pepsin were carried out in 24 cases. The results show a marked diminution in the peptic

TABLE II  
GASTRIC ACIDITY AND PEPSIN IN 26 CASES AFTER PARTIAL GASTRECTOMY

CASE	SEX	PRESENT AGE	LOCATION OF ORIGINAL ULCER	TYPE OF OPERATION	POSTOPERATIVE TIME INTERVAL	SYMPTOMS SINCE OPERATION	COLOR	EWALD TEST MEAL		
								FREE HCL	TOTAL ACID	PEPSIN MG. PER C.C.
1	F	57	Gastric	Polya (midgastric)	19 yr.	None	Yellow	12	37	1.2
2	M	39	Gastric	Bilroth II (pylorectomy)	15 yr.	None	Yellow	0	10	0.7
3	M	69	Gastric and duodenal	Bilroth II; Enterocenterostomy	15 yr.	None	Yellow	0	14	1.4
4	F	46	Duodenal	Bilroth II (pylorectomy)	14 yr.	Three periods of acute melena	Yellow	0	10	1.1
5	M	45	Gastric	Polya; enterocenterostomy	12 yr.	? jejunal ulcer	Clear	0	4	0.2
6	F	58	Gastric	Bilroth II	12 yr.	None	Yellow	0	8	--
7	F	47	Gastric and duodenal	Bilroth II (pylorectomy)	12 yr.	None	Yellow	0	8	0.9
8	F	57	Gastric	Anterior Polya (pylorectomy)	7 yr.	None	Yellow	0	10	--
9	F	27	Duodenal	Enterocenterostomy	7 yr.	None	Yellow	0	10	--
10	M	64	Gastric	Posterior Polya (pylorus)	7 yr.	None	Yellow	24	44	1.8
11	M	47	Duodenal	enterocenterostomy	6 yr.	None	Yellow	0	14	0.6
12	M	42	Gastric	Bilroth II	5 yr.	None	Yellow	0	16	0.0
13	F	64	Gastric	Enterocenterostomy	5 yr.	None	Yellow	0	16	0.2
14	M	31	Duodenal	Posterior Polya	3 yr.	None	Yellow	0	12	2.0
15	M	33	Duodenal	Anterior Polya	2 yr.	None	Yellow	0	16	0.8
16	M	54	Duodenal	Posterior Polya	2 yr.	None	Yellow	0	16	0.6
17	F	58	Duodenal	Posterior Polya	2 yr.	None	Yellow	0	8	0.0
18	M	41	Duodenal	Posterior Polya	2 yr.	None	Yellow	0	16	4.0
19	F	57	Gastric	Anterior Polya	1 yr.	Recurrent pain; marginal ulcer	Yellow	0	3	0.5
20	M	59	Duodenal	Anterior Polya	1 yr.	None	Yellow	0	24	0.1
21	M	41	Duodenal	Jejunal ulcer excised at subsequent operation	1 yr.	Jejunal ulcer excised at subsequent operation	Yellow	42	60	2.8
22	M	47	Duodenal	1 hemorrhage	1 yr.	1 hemorrhage	Yellow	0	8	0.2
23	M	33	Duodenal	None	1 yr.	None	Yellow	0	12	0.1
24	M	40	Gastric	None	6 mon.	None	Yellow	0	18	0.6
25	M	40	Gastric	Anterior Polya	4 mon.	None	Yellow	0	18	0.4
26	F	52	Duodenal	Anterior Polya	1 mon.	None	Yellow	0	10	0.3
				Posterior Polya	1 mon.	None	Clear	20	36	3.4

activity of gastric juice after partial gastrectomy in almost all instances. In all but 3 of our cases, the amount of pepsin was found to be below the range found in unoperated patients with peptic ulcer.\* In two instances no peptic activity was demonstrable. The specimens which contained free hydrochloric acid showed relatively large amounts of peptic activity, in accord with the usual finding of a proportionality between gastric acidity and peptic activity. No relation was apparent between the amount of pepsin secretion in individual cases and the postoperative time interval.

*Follow-Up Results.*—All of the patients included in this series have been carefully followed by the Surgical Clinic. Twenty-two members of the group, 12 of whom have been followed for over three years, have remained completely free from symptoms of ulcer during their entire follow-up period. The remaining four patients have suffered from recurrent abdominal pain or melena, attributed in each instance to jejunal ulcer. In one of these patients (Case 20) the presence of jejunal ulcer was proved at exploration. The gastric juice of this patient contained free hydrochloric acid. The other three patients (Cases 4, 18, and 21) who had had recurrent symptoms, however, showed anacidity. Our studies of gastric secretion offer no explanation for the therapeutic failure in these cases. In most instances, however, the occurrence of achlorhydria after partial gastrectomy for peptic ulcer offers a satisfactory explanation for the high percentage of successful results following that operation.

#### DISCUSSION

In the light of these findings several explanations for the reduced acidity resulting from partial gastrectomy may be considered. Gastric acidity depends upon the volume of acid secretion, the rate of emptying of the stomach and the presence of neutralizing or buffering substances. The finding of moderate amounts of combined acid and peptic activity in the majority of our cases indicates that the stomach usually continues to secrete in response to food after partial gastrectomy. It is impossible to determine directly the volume of such secretion. One can only surmise on the basis of animal experimentation<sup>1</sup> that a reduction in volume has occurred. Accelerated emptying of the test meal by the stomach after partial gastrectomy might be expected to decrease the period of gastric stimulation if the chemical phase of secretion is still partly effective. Our failure to obtain large volumes of gastric juice in most cases would suggest that the peak of secretion after the Ewald meal is passed in less than one hour. Admixture of alkaline juices from the small intestine is undoubtedly an important factor in reducing acidity after

\*The rough parallelism between acid and pepsin secretion is exemplified in un-complicated ulcer where the pepsin secretion tends to be high. The range of pepsin occurring in a series of patients with simple duodenal ulcer reported by Mullins and Flood<sup>12</sup> was 2.1 to 11.7 mg. per c.c. (U.S.P. pepsin 1:4,000). In gastric ulcer the results fall within the same range.<sup>13</sup>

partial gastrectomy and was *manifested* by the presence of intestinal juices in the gastric contents of nearly all of our cases.

The lowered peptic activity of gastric juice after partial gastrectomy may be attributed either to partial destruction of the enzyme or to diminished secretion. It is well known that the addition of alkali to an acid solution of pepsin irreversibly destroys pepsin. Thus, inactivation of pepsin by alkaline juices regurgitated from the intestine probably takes place after partial gastrectomy.

The evidence available supports the view that the anaecidity after partial gastrectomy is due both to a reduction in secretion and to regurgitation of alkaline intestinal juices. The relative quantitative importance of these two factors has yet to be determined. The marked lowering of the level of gastric acidity after partial resection affords a reasonable explanation for the high measure of success which this operation offers in the prevention of recurrences of peptic ulcer. The fact that ulcer may sometimes recur after operation in spite of this lowered acidity suggests that other unknown factors in addition to acid-pepsin digestion may play a role in the genesis of peptic ulcer.

#### SUMMARY

1. Gastric secretion after partial gastrectomy for peptic ulcer was studied in a series of 26 patients. Operation had been performed one month to nineteen years previously.

2. Twenty-two patients (85 per cent) exhibited achlorhydria after a test meal.

3. Gastric pepsin was markedly diminished in 21 of 24 cases studied (88 per cent).

4. Follow-up observations indicated in general that those patients with anaecidity remained asymptomatic. However, three patients with anaecidity had recurrent symptoms of ulcer.

5. The reduction in the level of gastric acidity occurring after partial gastrectomy explains the success of that operation in the prevention of recurrence of ulcer.

6. The reduced acidity is probably due both to the abolition of the chemical phase of gastric secretion and to regurgitation of alkaline intestinal juices.

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## TUBERCULOSIS OF THE STOMACH

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IT IS a curious fact that tuberculosis seldom attacks the stomach. For example, in the study of 1,400 autopsies upon tuberculous subjects, Crawford and Sawyer<sup>5</sup> did not find a single instance of gastric involvement; whereas, the incidence of tuberculous lesions of the ileum and colon reached 70 per cent. The remarkable resistance of the stomach to this infection becomes most impressive if we recall the routine clinical use made of the sputum to detect the presence of tubercle bacilli and recall also the fundamental character of the act of swallowing saliva, a necessity good manners imposes incessantly upon all of us, tuberculous or not. Clearly, potent bacteria reach the stomach often enough and in sufficient number to make a formidable attack upon that organ whenever individuals suffer from the commonplace respiratory types of tuberculosis. Why it does not happen so remains a moot question. Some distinguished pathologists have taught that the acidity of the gastric juice was the responsible protective factor; others have emphasized the rapid transportation of infectious material through the organ, an efficient degree of gastric motility. Of late it is the inclination of those giving the problem special study to point a close relationship between a low incidence of gastric tuberculosis and the meagre supply of lymphoid tissue in the wall of the stomach. In any case, a preliminary break in the continuity of the gastric mucosa seems essential to its penetration by the tubercle bacillus.

Rigid criteria for authentication of the pathologic diagnosis have served appreciably to limit the number of cases of gastric tuberculosis worthy of publication. From a review of the literature as far as 1917, Broders<sup>1</sup> gathered 307 presumptive cases, although the typical microscopic anatomy and acid-fast bacilli had been demonstrated only 50 times. In addition, the histologic evidence was adequate in 118 instances, but there no mention was made of the presence of organisms. Among the remaining cases, 59 were regarded as doubtful, while 89 were rejected altogether. Good<sup>3</sup> carried the compilation forward to the year 1931, collecting 194 cases which deserved consideration; in 52 the diagnosis was positive, in the others quite probable. Subsequently 17 completely established cases have been added to the list through the reports of Pop,<sup>2</sup> Price,<sup>4</sup> Genkin,<sup>6</sup> Knollbach,<sup>7</sup> Szaecsvay,<sup>8</sup> Grayzel,<sup>9</sup> Walters and others,<sup>10</sup> Eusterman and Balfour.<sup>11</sup> The analysis of all the material available thus far yields 54 cases definitely proved and 157 probable, a total of 211 cases in medical literature to the end of 1937.

The clinical manifestations of gastric tuberculosis vary with the way the tissues react to the invading organisms. Whenever the degree of cellular proliferation gives rise to a tuberculoma, both the symptoms and the roentgenologic findings resemble those associated with carcinoma. On the other hand, ulcerative lesions are productive of symptoms akin to those of peptic ulcer. Then again, but very rarely, miliary tuberculosis or tuberculous lymphangitis of the stomach may be encountered; in these circumstances no symptoms appear, at least none have been recognized. Pathognomonic roentgenologic details of gastric tuberculosis have yet to be described.

The demonstration of tuberculosis elsewhere in the body has not proved very helpful in the difficult task of differentiating gastric tuberculosis from carcinoma or from peptic ulcer. It is true, however, that roundly 50 per cent of the authenticated cases of gastric tuberculosis have occurred simultaneously with tuberculous foci in other organs, especially with the pulmonary variety.

Since there is slight, if any, disposition on the part of gastric tuberculosis to heal spontaneously and since with time its symptoms become more and more aggravating, occasionally surgical intervention has been required, as in the case herewith reported. The strength of the patient and the extent of the gastric lesion guide the surgeon in the type of operation he selects. Obviously, the more radical the resection, the greater the likelihood of eliminating the disease from the stomach. And, in a practical sense, nothing has been gained from the refinements of preoperative differential diagnosis, for the same technical principles prevail in the treatment here, as in peptic ulcer and carcinoma. A mortality of 21 per cent, according to Good, was associated with the operative treatment of 24 cases of gastric tuberculosis.

#### CASE REPORT

J. A. K. (No. 489-556), a Caucasian piano-maker, entered the Los Angeles County General Hospital, March 28, 1936. A mild, dry, nonproductive cough had persisted five years. There were no gastric symptoms until three years before admission, when he began to suffer from epigastric pain one to three hours after meals. This distress was relieved by drinking milk or beer.

Physical examination revealed signs of infiltration at the apices of both lungs, with cavitation on the left. Palpation of the abdomen disclosed a slightly tender mass 5 cm. in diameter in the left hypochondrium. By the benzidine test the stools were positive for occult blood. The sputum contained numerous acid-fast bacilli. Both the Wassermann and Kahn reactions were negative. Blood count: Hb. 75 per cent; R.B.C., 4,850,000; leucocytes, 9,400. Fractional gastric analysis with histamine gave a maximum total acidity of 50° and a free acidity of 32°. Urinalysis was negative.

Roentgenologic examination revealed no obstruction of the stomach, but there was a tender filling defect in the prepyloric region of the greater curvature, strongly suggestive of malignancy. There was chronic bilateral ulcerative tuberculosis of the lungs, far advanced.

The preoperative diagnosis included pulmonary tuberculosis and carcinoma of the prepyloric region of the stomach. On April 4, 1936, under cyclopropane, nitrous oxide, and avertin anesthesia, the abdomen was explored through a left paramedian incision. The viscera, other than the stomach, showed no abnormality. A grayish, infiltrating mass, approximately 5 inches long, was visible in the prepyloric region, and along the greater curvature numerous mesenteric lymph glands were enlarged. Grossly, the appearance of the lesion was suggestive of carcinoma, but upon palpation the mass was found less firm and not so thick as in the average case of carcinoma.



Fig. 1.—Tuberculosis of stomach; preoperative gastric x-ray.

A partial gastric resection was performed, removing a segment extending from 1 inch distal to 7 inches proximal to the pylorus. After closure of the duodenal stump, an antiperistaltic, retrocolic Polya anastomosis was made between the distal end of the stomach and the first portion of the jejunum. The abdomen was closed without drainage. The postoperative course was uncomplicated, save for slow healing of the wound, which finally closed completely. On July 4, 1936, no evidence of obstruction was found during roentgenologic examination of the stomach. On the other hand, the chest study showed an increase in the nodular infiltration of the



Fig. 2.—Tuberculosis of stomach; preoperative chest x-ray.

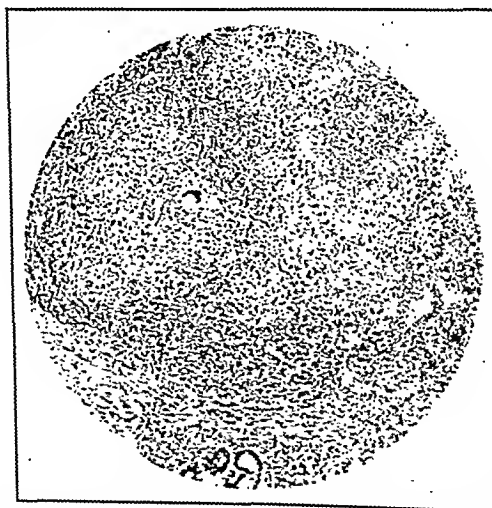


Fig. 3.—Tuberculosis of stomach wall, showing typical giant cell formation ( $\times 65$ ).

upper portions of both lungs since the examination preliminary to operation. Against advice, however, the patient left the hospital July 24. He died at home Aug. 21, 1936, of pulmonary tuberculosis.

Pathologic examination of the excised prepyloric portion of the stomach, made by Dr. Newton Evans, follows: "The specimen consists of the wall of a hollow viscus, apparently the stomach, which has already been divided and now measures 15 by 7 cm. From the outer surface, a small amount of mesenteric or omental tissue projects. An indurated area on the serosal surface measuring 4.5 cm. in diameter presents large numbers of minute nodules having the appearance of miliary tubercles. In this area the wall is thickened and corresponds to a shallow ulcerated area in the mucosa, which has indistinct margins and is poorly differentiated from the surrounding mucosa. Section across this area shows the wall which measures 1.5 cm. in thickness to be filled with miliary sized tubercles.

*Microscopic.*—Section through this involved area shows that the ulcer on the inner surface is shallow and does not extend much beyond the depth of the muscularis mucosa at any point. The ulcer surface is largely covered by a necrotic area of tissue with a small amount of superficial exudate. Scattered through all the remaining layers of the stomach are numerous rounded discrete and conglomerate tubercles having the characteristic morphology, including great numbers of Langhan's type of giant cells, but with almost no areas of definite caseation. Acid-fast stain of the tissue sections reveals numerous acid-fast bacilli having the typical morphology of tubercle bacilli. These are found within the tubercles, occasionally within the giant cells, and in considerable numbers in the granulation tissue immediately at the base of the necrotic ulcerated surface. No final conclusion can be reached as to the atrium of the infection in the stomach wall, but the impression is left that the infection probably began in the mucosa and extended through the lymphatics to all the tissue layers of the involved area of stomach wall.

*Diagnosis.*—Tuberculous ulcer and extensive miliary tuberculosis of the stomach wall."

#### SUMMARY

Tuberculosis does not attack the stomach very often, 211 definitely proved and quite probable cases having been reported to the end of 1937. To these is added a case in which a partial gastric resection was performed. The excised portion of the stomach wall contained an ulcer along with numerous miliary tubercles of typical structure, including giant cells and acid-fast bacilli. Pulmonary tuberculosis caused the patient's death four and one-half months after the operation.

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## A CRITICAL SURVEY OF PERITONEOSCOPY

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PERITONEOSCOPY, the direct inspection of the abdominal cavity by means of an optical instrument, is not a new procedure, as the cystoscope has for many years been used for this purpose. However, with few exceptions, preliminary reports only of peritoneoscopy have been published and rarely followed by further publications. It is difficult to understand this lack of sustained interest in view of the satisfactory results and the safety with which this procedure can be carried out. Ruddock<sup>1</sup> again has reviewed the problem and described a new instrument which is more readily used than the cystoscope. His series of 500 cases, by far the most complete now available, has helped to recreate an interest in this subject. In this country Horan<sup>2</sup> and Benedict<sup>3</sup> recently have published series of fifty observations each, while Hope,<sup>4</sup> Anderson,<sup>5</sup> Findlay,<sup>6</sup> Stolze,<sup>7</sup> and others have issued preliminary reports.

Because of the diagnostic possibilities of peritoneoscopy, it was decided at the University Hospital to investigate its value and cases were carefully selected. All observations were carried out by one person so as to gain a uniform impression of the indications, technique, and results. During the past six months, peritoneoscopy rarely has been used as the preliminary study in this series, but it has been resorted to after inconclusive diagnosis had been made by other means, or when biopsy, or the operability of a clinically suspected neoplasm, was desired. The number of cases has greatly increased as the value and safety of peritoneoscopy have been demonstrated. It has come to be considered a valuable final authority in diagnosis, equal in many instances to laparotomy and having only a fraction of the expense or morbidity of a major operation.

### TECHNIQUE

The technique used is essentially that described by Ruddock<sup>1, 8</sup> and subsequently by many others. The instrument set used was illustrated in his article and is now known as the Ruddock peritoneoscope. Patients are prepared as for laparotomy and all examinations are carried out aseptically. We have found that an enema followed by 1 c.c. of pitressin (Horan<sup>2</sup>) aids greatly in reducing intestinal volume, thus allowing more room for observation. Morphine sulfate was the only sedative used. One per cent procaine local anesthesia was used in all but one instance, the

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upper portions of both lungs since the examination preliminary to operation. Against advice, however, the patient left the hospital July 24. He died at home Aug. 21, 1936, of pulmonary tuberculosis.

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*Diagnosis.*—Tuberculous ulcer and extensive miliary tuberculosis of the stomach wall."

#### SUMMARY

Tuberculosis does not attack the stomach very often, 211 definitely proved and quite probable cases having been reported to the end of 1937. To these is added a case in which a partial gastric resection was performed. The excised portion of the stomach wall contained an ulcer along with numerous miliary tubercles of typical structure, including giant cells and acid-fast bacilli. Pulmonary tuberculosis caused the patient's death four and one-half months after the operation.

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not been forced to laparotomy either by bowel perforation or by hemorrhage, but it is undoubtedly only a matter of further experience before this occurs.

#### ACCURACY OF DIAGNOSIS

Based on this particular series it is impossible to draw numerical conclusions concerning the accuracy of diagnosis by peritoneoscopy compared to the clinical acumen of the hospital at large. In one large group of cases the clinical impression was fairly certain and peritoneoscopy served only to confirm the diagnosis, secure a biopsy, or estimate operability. Had peritoneoscopy alone been employed, one cannot say how accurate it might have been. In another large group of cases complete clinical studies had failed to reach a conclusive diagnosis, although supplying negative information. Peritoneoscopy was expected to select the proper diagnosis from an array of clinical possibilities presented by a large teaching staff. Obviously some clinical would be correct, although no one clinician could afford to be certain. Peritoneoscopy settled the diagnostic problems in these situations in a high percentage of cases.

#### DISCUSSION OF CASES

Only cases that had been thoroughly studied by other means were accepted for peritoneoscopy, although, as its value has been demonstrated, it has occasionally been used as a short cut to diagnosis. No patient whose condition did not offer a definite question for answer was examined. With the indication for peritoneoscopy as a classification, the cases may be divided into the following general groups:

I. Liver-spleen syndromics: Includes biliary tract pathology, primary liver disease, and enlargements of both liver and spleen of unknown etiology.

II. Suspected abdominal malignancies: These were clinically diagnosed as malignancies, but confirmatory biopsies were desired, or the primary site or operability was questioned.

III. Identification of unknown masses in the abdomen.

IV. Ascites of unknown origin.

V. Tuberculous peritonitis.

We have not been asked to diagnose ectopic pregnancy nor to see many patients for other gynecologic complaints. As cautioned by Rudock, we have avoided all acute abdomens.

*Group I. Liver-Spleen Syndromics (15 Cases) (Table I).*—Clinical diagnosis in the problem of jaundice or of hepatosplenomegaly rarely can be accurate, but it must be obtained to guide rational treatment. Peritoneoscopy, with none of the dangers of laparotomy, gave an accurate working diagnosis in 14 cases. In the fifteenth (Case 2) an early carcinoma at the head of the pancreas was diagnosed as a common duct stone and laparotomy was advised. This advice was not followed as



second. This patient complained so bitterly of pain during the movement of the instrument that gas anesthesia was used. In retrospect, it is apparent that only the site of puncture was anesthetized. Since then local infiltration has been carried to all layers in an area of 6 to 10 cm. from the puncture site. This has allowed greater distention of the abdomen and painless manipulation of the instrument. The incision has generally been placed in the rectus muscle at the level of the umbilicus, although this has varied according to local pathology. A nick in the fascia is routinely made to facilitate the introduction of the large trocar. Room air of an unknown quantity and pressure is used for the pneumoperitoneum. No respiratory difficulties were encountered, although overdistention was occasionally accompanied by nausea. Observation was successful in all instances but occasionally was limited by adhesions, particularly in those patients who had undergone previous surgery. Considerable skill can be attained in maneuvering in and out among adhesions. Walls of adhesions too long to circumvent can be pierced and observation carried beyond. We have never attempted to cut adhesions as a therapeutic measure. In no case was it necessary to re-examine a patient because of inadequate observations.

Shifting the patient's position will frequently help to visualize the superior surface of the liver or pelvis. Transillumination of the stomach has not been uniformly successful. It has been helpful to distend the stomach with air by means of the Rehfuess tube. Peristalsis is thus initiated and its course through the stomach observed. The duodenum is brought into relief and is fairly well visualized by this distention. We have not used cystoscopy or sigmoidoscopy in conjunction with our examinations as suggested by Ruddock. After the initial 10 cases, biopsy was attempted whenever indicated. Of the 14 cases in which the clinicians desired biopsy, we were able to do so in 12. Failures were in liver biopsies where tissue taken for examination was inadequate or too mutilated. After preliminary cauterization of overlying blood vessels, it has been found feasible to obtain bits of mesenteric lymph node. A uniform plan of observation was followed, beginning in the right upper quadrant and passing around in a clockwise direction. Complete examinations were done in all cases. Unless enlarged, the spleen was seldom seen and the appendix was rarely found.

#### COMPLICATIONS

To date there has been no mortality or morbidity. Patients not confined to bed by the primary disease have been allowed up on the same or the following day. Three have complained of transitory shoulder pain. A hematoma has occurred in the wounds of two deeply jaundiced patients. One woman with a six-inch panniculus and uncontrolled diabetes mellitus suffered a minor wound necrosis. Thus far we have

the patient died. The patient's course would not have been adversely affected, had he lived, because of the erroneous diagnosis. Lesions at the head of the pancreas can only be seen peritoneoscopically if they are far enough advanced to have metastasized or to have pushed up from the retroperitoneal spaces. However, the liver and gall bladder can be readily inspected and an intelligent correlation of what is seen, we believe, will give the correct answer. In contrast to this one mistaken diagnosis made by peritoneoscopy, clinical diagnoses were wrong in three instances. The subsequent course of these three patients was altered by the change in diagnosis: Case 7 received treatment for cirrhosis with ascites rather than palliation for abdominal carcinomatosis; Case 6 was saved from laparotomy; and Case 9 had an elective herniorrhaphy after the clinical diagnosis of cirrhosis with ascites was corrected.

Laparotomy was the last recourse to establish a positive diagnosis in all 15 cases. This major operation was eliminated in 7 of the 15 cases. In an eighth, laparotomy was not advised but was done because of lack of confidence in the peritoneoscopic diagnosis. Surgery was carried out in the remaining 6 cases as suggested and was found to be the procedure of choice.

We feel from our brief experience that peritoneoscopy accurately answers the diagnostic problem and indicates the therapeutic approach in jaundice and in hepatosplenomegalies.

*Group II. Suspected Abdominal Malignancies (17 Cases) (Table II).—*Eight of these were carcinoma of the stomach, a small percentage of the total gastric malignancies seen in University Hospital during this six months' period. More gastric neoplasms were not examined because of lack of confidence in peritoneoscopy. We have never felt that clinical findings alone could accurately disclose the inoperable carcinoma of the stomach but we now know that peritoneoscopy can save many of these patients from operation. Therefore, we feel that peritoneoscopy should be done on all gastric neoplasms. The borderline cases will always come to operation. Three of the 8 patients with carcinoma of the stomach were saved from operation, but only 2 of the 5 considered operable were submitted to gastric resection.

Eight of the remaining 9 cases in this series were considered clinically to have abdominal malignancies. The ninth was a case of proved carcinoma of the rectum with a question of metastases to the liver, which were found by peritoneoscopy. Routine peritoneoscopy was considered for the large group of rectal neoplasms seen at the University Hospital, but this was rejected because the majority of these cases, whether operable or not, require a colostomy. Clinical diagnosis of abdominal malignancy in 5 of the 8 cases was established. Two had no malignancy at all and 1, by peritoneoscopy, was thought to have an operable carcinoma of the ovary, which at operation was found to be endometriosis of the tube and ovary. Peritoneoscopic examination, although mistaken in the

TABLE I  
LIVER-SPLEEN SYNDROMES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERTONEOSCOPY	DIAGNOSIS BY PERTONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
1 No. 365469	Jaundice, carcinoma, or common duct stone	Etiology of jaundice	Carcinoma at head of pancreas, no liver metastases	Adenocarcinoma, metastatic from breast	Previous radical mastectomy, no local recurrence; death, 6 weeks
2 No. 417742	Jaundice, carcinoma, or common duct stone	Etiology of jaundice	No carcinoma, probably common duct stones	None	Autopsy: small carcinoma at ampulla of Vater, no metastases
3 No. 414175	Jaundice, carcinoma at head of pancreas	Etiology of jaundice	Cirrhosis of liver, no cholecystitis	None	Cholecystectomy, normal gall bladder, liver biopsy, atrophic cirrhosis
4 No. 297271	Catarrhal jaundice or cirrhosis	Etiology of jaundice	Cirrhosis of liver, chronic cholecystitis	None	Cholecystectomy, ulcerative cholecystitis; liver biopsy, severe portal cirrhosis
5 No. 425525	Jaundice, carcinoma at head of pancreas	Etiology of jaundice	Carcinoma at head of pancreas	From liver, carcinoma	Cholecystogastrostomy
6 No. 419394	Jaundice, cirrhosis, or malignancy	Etiology of jaundice	Normal liver and gall bladder, catarrhal jaundice	None	Clinical course and subsequent x-ray; confirm diagnosis four months later
7 No. 421344	Jaundice, generalized carcinomatosis	Etiology of jaundice (?) primary	Cirrhosis with ascites, no malignancy	None	Improved with medical regime three months later
8 No. 415782	Jaundice, hepatosplenomegaly	Etiology of jaundice	Biliary obstruction, no cirrhosis or malignancy	None	Stricture of common duct; hepatosplenomegaly reduced with common duct drainage
9 No. 398184	Cirrhosis with ascites	Diagnosis	No ascites, no cirrhosis	None	Effective herniorrhaphy three months later
10 No. 418132	Hepatomegaly, no jaundice	Etiology of hepatomegaly	Metastatic malignancy (?) from head of pancreas	Adenocarcinoma mucosum in liver	Primary undetermined
11 No. 137681	Hepatomegaly	Etiology of hepatomegaly	No hepatomegaly, large inflammatory mass in right upper quadrant	None	Carcinoma of gall bladder; no metastases; large abscess
12 No. 171650	Hepatomegaly (?) gramma	Diagnosis	Large neoplasm in liver	None	No further information as yet
13 No. 419132	Hepatosplenomegaly (?) Banti's disease	Diagnosis biopsy	Cirrhosis of liver, chronic cholecystitis	Unsuccessful	Cholecystectomy; chronic cholecystitis; biopsy, atrophic cirrhosis
14 No. 419922	Hepatosplenomegaly	Etiology of hepatomegaly	Metastatic carcinoma (?) from head of pancreas	Inadequate from liver	Primary undetermined
15 No. 420998	Splenomegaly	Etiology of splenomegaly	Severe toxic hepatitis with splenomegaly	Inadequate from liver	Splenectomy, anemia infarcts; liver biopsy, atrophic cirrhosis

diagnosis in the last case mentioned, indicated the proper therapeutic approach in all 8. The clinical impression was definitely in error in the two cases shown not to have malignancy. Although previously laparotomy would have been necessary to gain the above information in all 9 cases, it probably would not have been carried out in 2 of the advanced malignancies.

We have concluded from this small group of 17 cases of abdominal malignancy that peritoneoscopy can save many patients from operation by eliminating the inoperable carcinoma of the stomach, establishing the diagnosis of abdominal carcinomatosis, and evaluating the extent of pelvic neoplasms. Treatment can be logically planned with the information thus gained by peritoneoscopy.

*Group III. Identification of Unknown Masses in the Abdomen (Table III).*—The clinically described mass was identified with certainty in only 6 of the 11 cases. In a case of testicular tumor it was quite certain that there was no abdominal mass as felt clinically. In the remaining 4 no accurate diagnosis could be made by peritoneoscopic findings because of the retroperitoneal position of the masses. Three of these 4 subsequently came to operation.

Three of the 11 would never have come to operation. Peritoneoscopy was used to identify retroperitoneal masses in 2 for whom surgery was not indicated; in the third it was used as a diagnostic shortcut, hardly the method of choice, to diagnose a hypernephroma, which was a clinical diagnostic error.

Laparotomy was probably inevitable in 8 of the 11 cases. It was eliminated in 2 because of carcinomatosis. Of the 6 operated upon, surgery had been correctly advised by peritoneoscopic examination in 5 but with only 3 correct diagnoses. In the sixth case no abdominal mass and no surgical lesion were found, a clinical and surgical error.

We feel that peritoneoscopy will do little to identify retroperitoneal masses. It will aid in locating intra-abdominal masses and will eliminate laparotomy in those having advanced abdominal malignancy. Therefore this examination for unidentified abdominal masses must be recommended with reservations.

*Group IV. Ascites of Unknown Origin, 3 Cases (Table IV).*—Biopsy by peritoneoscopy proved carcinomatosis in 2 cases and in the third an accurate diagnosis was not made. Three months later autopsy showed an intrahepatic neoplasm in this third case. With thorough clinical studies before peritoneoscopy, this group of ascites of unknown origin will continue to be small, but peritoneoscopy may be expected to give the correct diagnosis.

*Group V. Tuberculous Peritonitis, 4 Cases (Table V).*—The diagnosis of well-advanced tuberculous peritonitis was established by peritoneoscopy by 2 cases. The other 2 patients presented vague abdominal complaints with clinical diagnosis of intestinal or peritoneal tuberculosis,

TABLE II  
ABDOMINAL MALIGNANCIES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
No. 423641	Carcinoma of stomach	(?) Operability	Operable	None	Laparotomy: carcinoma too high on lesser curvature Death three weeks later
No. 419893	Carcinoma of stomach	(?) Operability		Adenocarcinoma	Slowly down hill
No. 416773	Carcinoma of stomach	(?) Operability		None	No further information
No. 422457	Carcinoma of stomach	(?) Operability		Carcinoma	Laparotomy; not resectable
No. 424370	Carcinoma of stomach	(?) Operability	No metastases but locally extensive lesion	None	Gastric resection
No. 424888	Carcinoma of stomach	(?) Operability	Operable	None	Laparotomy, no pelvic neoplasm, gastric resection neurofibroma
No. 424574	Krukenberg tumor	Confirm diagnosis	No malignancy in pelvis, (?) the malignancy in the stomach	None	Inoperable due to involvement of posterior wall of stomach Transverse colostomy only
No. 417303	Previous excision of malignant ulcer	(?) Recurrence of gastric neoplasm	Metastases to liver	None	Palliative x-ray therapy
No. 423318	Proved carcinoma of rectum	(?) Abdominal metastases	Carcinoma of right ovary	Cystadenocarcinoma	Failing rapidly
No. 419415	Carcinomatosis (1), origin in pelvis	Diagnosis biopsy	Carcinoma of left ovary	Carcinoma	Death three weeks later
No. 411798	Carcinomatosis (1), origin in pelvis	Diagnosis biopsy	Abdominal carcinomatosis	None	No further information
No. 408257	Ascites (1), recurrent carcinoma of the stomach	Diagnosis	Abdominal carcinomatosis (3) origin in retroperitoneal mass	None	Autopsy: carcinoma, primary in terminal ileum Discharged on conservative regimen
No. 421510	Generalized carcinomatosis	(1) Origin	Abdominal carcinomatosis arising at head of pancreas	Unsatisfactory from liver	No change three months later
No. 423045	Abdominal carcinomatosis	(1) Origin	Negative abdomen, chronic pelvic inflammation	None	Laparotomy: endometriosis of tube and ovary
No. 424077	Carcinomatosis (1), origin in pelvis	Diagnosis	No malignancy, fibroid uterus, cystic ovary	None	
No. 420510	Obesity (1), pelvic neoplasm	Diagnosis, (?) operability	Carcinoma of right ovary, operable	None	
No. 333824	(1) Pelvic neoplasm	Diagnosis, (?) operability			

TABLE IV  
ASCITES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
44 No. 415162	Ascites	Etiology of ascites	(?) Syphilitic hepatitis, no malignancy	None	Autopsy: carcinoma of large bile ducts, no metastases except deep in liver
45 No. 422732	Ascites, mass in left upper quadrant	Etiology of ascites	Abdomen full of mucin from an adenocarcinoma mucosum	Mucin from adenocarcinoma mucosum	Peritoneoscopy used as the initial and only study
46 No. 331846	Ascites; 3 years post-operative radical breast	Etiology of ascites, (7) carcinomatosis	Carcinomatosis of peritoneum only	Diffuse carcinomatosis	Death three months later

TABLE III  
ABDOMINAL MASSES

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATIONS FOR PERTONEOSCOPY	DIAGNOSIS BY PERTONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
33 No. 419002	Mass in right midepigastrium	Identification of mass	Negative except for (?) mass about duodenum	None	Laparotomy: carcinoma at head of pancreas without metastases
34 No. 419822	Mass in right upper quadrant	Identification of mass	Chronic cholecystitis, no carcinoma	None	Laparotomy: chronic cholecystitis and lithiasis
35 No. 422481	Mass in right upper quadrant, postoperative cholecystectomy	Identification of mass	No carcinoma (?) mass at head of pancreas	None	Laparotomy: adhesions only from previous surgery
36 No. 423560	Mass in right upper quadrant	Identification of mass	No carcinoma, chronic cholecystitis	None	Laparotomy: chronic cholecystitis and lithiasis
37 No. 419642	Retropertitoneal sarcoma	Identification of mass in epigastrium	Retropertitoneal mass without metastases	None	Laparotomy: carcinoma of cardia of stomach
38 No. 417310	Mass extrinsic to stomach	Identification of mass	Inoperable carcinoma of stomach	None	Death three weeks later
39 No. 422004	Mass epigastrium, (?) neoplasm in lungs	Identification of mass, (?) carcinoma	No carcinomatosis, mass near body of pancreas	None	No further information from other studies
40 No. 420672	Large mass in right abdomen	Identification of mass, (?) carcinoma	Hypernephroma	None	Pyelograms positive; peritoneoscopy used as a diagnostic short cut
41 No. 417413	Low abdominal mass, (?) carcinoma from ovary	Biopsy, identification of mass	Pelvic abscess, no malignancy	None	Laparotomy; pelvic abscess
42 No. 410671	Middle abdominal mass, (?) carcinoma from ovary	Identification of mass	Carcinomatosis arising in right ovary	From peritoneum, adenocarcinoma	Palliative x-ray therapy
43 No. 400404	Postoperative tumor of the testicle	Abdominal mass or metastases	No abdominal mass, no liver metastases	None	No further treatment, but to be observed

In neither of these 2 could the diagnosis be confirmed. We hope to be able to re-examine the 2 patients of proved tuberculous peritonitis at intervals as much may be learned of the disease in this manner.

#### SUMMARY

Peritoneoscopy has been done on fifty patients. The cases are reported herein in detail as a critical survey of this method of examination. We have found it to be entirely safe and very accurate, supplying much of the information usually gained by laparotomy, with none of the expense or morbidity of a major operation. Satisfactory biopsies may be obtained with little additional risk to the patient.

Peritoneoscopy will give an accurate diagnosis and indicate the treatment in cases of jaundice and hepatosplenomegaly. It should be used routinely in carcinoma of the stomach to avert operation in the inoperable cases. The extent of pelvic and abdominal neoplasms can be accurately estimated for proper treatment. It cannot be expected to identify retroperitoneal masses unless they are far advanced. Abdominal tuberculosis can be readily diagnosed and its course should be followed by repeated peritoneoscopic examinations. Many patients with a presumptive clinical diagnosis which would contraindicate operation can be safely examined by peritoneoscopy and receive the benefit of treatment based on correct diagnosis. These diagnoses may be at variance with the clinical diagnoses and may change the prognosis entirely.

In short, we feel that every large teaching hospital should have one of these instruments for diagnostic studies.

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TABLE V  
ABDOMINAL TUBERCULOSIS

CASE NUMBER	CLINICAL DIAGNOSIS	INDICATION FOR PERITONEOSCOPY	DIAGNOSIS BY PERITONEOSCOPY	BIOPSY	SUBSEQUENT COURSE
47 No. 413591	Pelvic tuberculous	Diagnosis	Pelvic tuberculous	None	Guinea pig negative; still in Sanatorium
48 No. 422757	Tuberculous peritonitis	Diagnosis	Peritoneal tuberculous; generalized; no adhesions	Active tuberculous	Smears and cultures negative
49 No. 413229	Tuberculous peritonitis, operative diagnosis elsewhere	Diagnosis	Negative abdomen	Negative mesenteric lymph gland	Continues to have vague abdominal distress
50 No. 331749	Postoperative thoraco-plasties, (?) intestinal tuberculous	Diagnosis	Negative abdomen	None	Continues to have same vague abdominal complaints

TABLE I

DATE	AUTHOR	NO. OF CASES	SOLUTIONS USED	METHOD AND RESULTS
1835	Velpeau <sup>3</sup>	3	Iodine	Flushed hernial sac through incision in serotum; all 3 cases cured
1836	Pancoast <sup>4</sup>	13 in 8 yr.	Lugol's solution. Tr. cantharides	Used syringe and cannula; all cured
1840	Jayne <sup>5</sup>		Essential oils. Tr. cantharides	Special patented instrument; claimed 75 per cent cures
1841	Heaton <sup>6</sup>		Secret at first. Solution quereus albus	Special syringe and needle; disfavor of American colleges due to secrecy of method; claimed too much (100 per cent cures [?]); only one injection given; patient put to bed and bandage applied
1877	Schwalbe <sup>7</sup>		70 per cent alcohol	Daily injections for about two weeks; patient kept in bed
1881	Warren <sup>8</sup>		Quereus albus	Disciple of Heaton; only one massive dose given and patient confined to bed; first to describe rationale of seroplastic tissue repair; recommended painting inguinal rings and canal with solution during surgical operation (80 to 85 per cent cures)
1892	Marcy <sup>9</sup>			Discussed injection treatment in monograph on hernia
1893	Manley <sup>10</sup>			Emphasized proper selection of cases
1900	Pina Mestre <sup>11</sup>	15,000 (20 yr.)	Pina Mestre	Claims inguinal closed in 10 to 15 days (98 per cent cures)
1900 to 1932	Mayer <sup>12</sup>	21,000 (30 yr.)	Zinc sulph. phenol and alcohol	First to make treatment ambulant; 98 per cent cures; 2 per cent cured subsequently; small doses; patient wore truss during treatment
1904	Wollerman <sup>13</sup>	554	Alcohol (?)	92 per cent cure
1907	Lanne-longue <sup>14</sup>		10 per cent zinc chloride	Very enthusiastic about its use in hernia injection after noting its effect on stimulating growth of fibrous tissue in tuberculous deposits
1928	Steffen <sup>15</sup>	2,775 (30 yr.)	Alcohol	One injection weekly for 1 year; no deaths in 30 years of treatment (91.2 per cent cures)
1929	Wyss <sup>16</sup>	Review of 4,632	Alcohol	3,084 follow-ups; 91 per cent cures; no vital damage; 4 per cent complications (abscess, orchitis, hydrocele, atrophy of testis)
1929	Hall <sup>17</sup>	33	Pina Mestre	Histologic work on animals (peritoneal injections); formation of adhesions and a connective tissue barrier, thus effectively blocking and obliterating the canal; 1 failure

## TECHNIQUE OF THE INJECTION TREATMENT FOR INGUINAL HERNIA

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IT IS a long time since Billroth prophesied that if a solution could be perfected which would cause the proliferation of connective tissue when injected into the inguinal canal, then the treatment of hernia in a large measure would be simplified. This prophesy is being fulfilled. Solutions have been evolved which produce sclerosis in a safe manner, as described by one of us (H. I. B.) in a previous article.<sup>1</sup> This is not sufficient, however, to place this therapy on a firm footing. It is important, in addition, to develop a sound technique in order to make the method efficient and enduring.

It will serve no purpose to repeat the historical summaries of previous writers. Most of this work has been repetitions, as pointed out by Crohn.<sup>2</sup> For those who are interested in the chronological growth of this method, we have arranged a chart, Table I. This historical summary shows that the method has been in use for practically one hundred years. It has waxed and waned in popularity during the past century depending upon the character of the men into whose hands it fell. A more favorable background has been developed recently, as a result of important histological studies<sup>3,6</sup> and improved solutions. The important point at the present time is that there is still room for improvement in technique. It is the purpose of this paper to describe an injection method which is based upon sound principles.

A review of the literature shows a lack of interest in detailed or standardized technique. Those authors who mention technique do so in a general way and favor angles of injection that seem to the authors essentially unsafe. The entire crux of the problem lies in the proper conception of what takes place with injection therapy. What is aimed at is adhesion between important structures as the result of fibrous tissue growth. This fibrous proliferation following chemical irritation is a definite fact which has been proved and confirmed by previous workers. It must be emphasized that the object is not scar tissue as such, because it is perfectly possible to create huge lumps of dense fibrous tissue and get a complete failure. What is aimed at, rather, is permanent adhesion of weakened to relatively normal structures as the result of fibrous union. It is, therefore, of the utmost importance to place the needle point in the proper fascial plane by a definite orderly and sys-

TABLE I—CONT'D

DATE	AUTHOR	NO. OF CASES	SOLUTIONS USED	METHOD AND RESULTS
1936	Girard <sup>33</sup>	174	Tannic acid, phenol, and alcohol; thuja solution; sylvanacol, Pina Mestre	Series included 19 postoperative recurrences; also injected postoperative repairs with threatened weakening; claims recurrences in injected cases due to undertreatment
1936	Gordon and Gordon <sup>34</sup>	5		Contraindication of injection treatment in sliding hernia; present in 1.2-1.5 per cent of cases seen; injections, however, do not interfere with operative procedure or result
1937	Crohn <sup>2</sup>		Phenol, alcohol, and oil of thuja	Confirmed Rice's histologic work; no serious complications
1937	Rea <sup>35</sup>			Reviewed 75 cases injected for unilateral inguinal hernia and found only one case of delay in libido; followed 26 cases injected for bilateral inguinal hernia for 3 years and found normal spermatoc count; no sterility

tematic plan. At the completion of the case a line of adhesions will be formed in much the same manner as after a thorough surgical operation.

The points of adhesion that are produced by this method are not completely understood. From the few operative reports presented in the literature,<sup>34</sup> and from our personal clinical observations, it would seem that one point of adhesion is between the aponeurosis of the external oblique and the underlying internal oblique muscle. There is evidence at hand to show adhesions between conjoined tendon and the overlying fascia of the spermatic cord and external oblique muscle. There are other points of adhesion following this treatment which resemble largely those following operative methods. However, much work is necessary before more definite statements can be made. It may be pointed out in general that the adhesions aimed at involve fascial structures, because it has been shown recently<sup>37</sup> that adhesions of fascia to muscle are at best temporary and evanescent.

In studying the evolution of the modern operation for inguinal hernia, one is impressed by the multiplicity of procedures which have been and are still being used. It is evident from this that no single method is without criticism. More important still, the trend of the new operations points out clearly the defects inherent in the older surgical approach. The operative treatment of hernia has been taken for granted by the majority of the profession in the past. For a long time no proper study was made of the permanent planes of adhesion following surgical repair. Other problems in connection with the etiology and recurrence of hernias have not been solved. The mechanics of the musculofascial

TABLE I—CONT'D

DATE	AUTHOR	NO. OF CASES	SOLUTIONS USED	METHOD AND RESULTS
1930	Goldbahn <sup>18</sup>		Alcohol	Reported results of unskilled injections in cases of strangulated irreducible hernias, resulting in sepsis, fecal fistulas, and deaths
1930	Jameson and Cantala <sup>19</sup>	64	Pina Mestre	12 to 15 daily injections; claim it is the method of choice in cases of recurrent hernia
1931	Wolfe <sup>20</sup>	22	Pina Mestre	Described seroplastic exudation and formation of adhesions in inguinal canal; injected into peritoneum of animals and produced plastic peritonitis; claimed vas not injured if cord injected
1932	La Rochelle <sup>21</sup>		Pina Mestre	Injections should supplement operative treatment, help produce internal tissue pad or truss
1933	McKinney <sup>22</sup>		Phenol, alcohol, oil of thuja	Production of fibroblasts (without necrosis) in adjoining muscle tissue
1934	Larson <sup>23</sup>	137	Phenol, alcohol, and thuja solution	8 injections; injection treatment suitable in 90 per cent of cases seen (93.5 per cent cures); no serious complication
1934	Gray <sup>24</sup>	20	Mayer's solution	75 per cent cure
1934	Bratrud <sup>25</sup>	406	Tannic solution	4 per cent recurrences with three final failures; animal injections; marked fibroblast proliferation, no polymorphonuclears, giant cells, or necrosis
1934	Rice <sup>26</sup>	600	Phenol, alcohol, and oil of thuja, sodium psyllate	2 failures; no severe complications; histologic work on biopsy specimens from injected cases at operation shows dense adult fibrous tissue present by the forty-second day after injection
1935	Fowler <sup>27</sup>	700 (5 yr.)	Tannic and gallic acids	98 per cent cure, no serious complications; advised initial overbuilding of tissue to allow for absorption
1935	Fantus <sup>28</sup>			Believes certain percentage of reducible hernia curable by injection
1935	Quillin <sup>29</sup>	242		210 indirect, 4 direct, 23 recurrent, 5 umbilical; work and investigation on cadaver
1935	Kretschmar <sup>30</sup>	140		Points out infections close hernial sac same as nature closes processus vaginalis
1936	McMillan <sup>31</sup>	400	Thuja solution, tannic acid	8 per cent recurrences; no serious complications
1936	Zieman and Larkowski <sup>32</sup>	1	Tr. of thuja	Report necrosis of cord structures with swelling of vas after one injection

where one takes advantage of adhesions to the fascial insertions on the pubic bone. It can thus be seen that a good technique for the injection treatment of hernia must take into consideration numerous factors and it is not the simple procedure that previous authors have described.

### TECHNIQUE

The equipment required is as follows: (1) Iodine, alcohol, applicators, gauze sponges and pads; (2) syringes: one 2 c.c. and one 5 c.c. glass syringe; (3) needles: 25 gauge 3/4-inch needles for anesthesia; 3- and 4-inch 20 gauge needles for deep injection; (4) solutions: .2 per cent procaine without adrenalin, sylnasol, monolate, proliferol, neogal-tanol.

The patient is prepared for each injection by having him void so as to make certain the bladder is completely empty. The actual injection is performed with the patient lying supine and completely relaxed on a flat table. In this position the operator removes the truss and outlines the inguinal canal.

For practical purposes, the location of the inguinal canal is gauged by various means. Manual examination with one finger in the external ring is the simplest way. Noticing the shape of the bulge on cough is another means. Occasionally, the structures of the cord may be palpated for half the distance of the canal. In the spare subject, the course of the femoral artery and its branch, the deep epigastrie, may be traced where it enters the internal ring. By the aid of all these factors, the inguinal canal may be mapped out with a fair degree of accuracy. The senior author's new method of studying the inguinal canal with the use of radiopaque solutions, which is reserved for a future paper, will probably prove to be the most exact manner of visualization.

### INDIRECT HERNIA

The internal ring is usually first attached. The average location of this structure in the normal case has classically been described as one-half inch above the midpoint of a line drawn between the anterior superior spine and the pubic spine (Fig. 1). This is subject to individual variation and, in the presence of hernia, to considerable distortion. Therefore, in order to locate this structure, it is first necessary to outline the canal as previously described.

The actual injection of the internal ring is performed as follows: The location of the ring is marked with iodine. After preliminary skin anesthesia, the needle point is inserted approximately 1½ inches lateral to this point on the prolongation of a line running through the inguinal canal. The needle point is depressed so that it reaches the external oblique fascia slightly above the margin of the internal ring (Fig. 3) and, after penetrating the fascia, is continued in the same direction through the internal oblique muscle to the transversalis fascia. The

supports have never been clearly understood. The sphincterlike mechanism at the external ring has not been clearly elaborated. It has remained for the injection treatment of hernia to stimulate interest on these important points and lead the way for more rational therapy by both methods in the future.

Concretely, in comparing modern injection therapy with the latest endofascial approach,<sup>38</sup> one is impressed by the fact that both procedures aim at the same end result. In view of the fact that both methods produce adhesions in identical planes between similar structures, it may be concluded that theoretically, in properly selected cases, the injection method is superior to the operative procedure. The open technique involves division of fascia, muscle, nerves, and blood vessels and must weaken structures which are not normal to begin with.

Before attempting to do injection therapy, one should acquaint himself with the detailed anatomy of the inguinal region. This can only be done by repeated cadaver injection and dissection. Study of dye injection and minute anatomy of the canal itself forcibly emphasizes the fact that important structures are only fractions of centimeters away from the needle point. None of the techniques previously published have taken into account these dangers. The method to be outlined recognizes the hazards involved and the injection angles it describes are the safest ones that accomplish the desired result. The basic foundation of this technique rests upon the fact that a needle pointed toward the pubic spine will avoid most of the important structures in the inguinal region.

The manual dexterity acquired with the needle and syringe is indispensable and comes only after considerable clinical experience. Cadaver work, while essential, is only the preliminary phase of training, because the feel of the needle in dead tissue differs from that of the living. The best background for this special sclerosing technique is familiarity with injection treatment of varicose veins, hydrocele, and internal hemorrhoids.

Before leaving the subject of cadaver work, one should mention a rather interesting observation. It was noted that the colored fluid, although injected at one point of the inguinal canal, was found on dissection to have diffused over a wide area. This diffusion along the canal should not mislead the observer, because the spreading occurs only in one fascial plane and in all probability has very little action upon the fascia which lies either above or below it. For this reason, it is considered advisable in the actual injection to move the needle point so as to enter as many planes as possible during the treatment.

Careful study also brings out the fact that for permanent anchorage it is necessary to deposit irritating solutions not only in the canal itself but outside it. This is especially true in the case of direct hernia,

direction of the needle point, as in subsequent injections, is toward the pubic spine and the angle that the needle makes with the inguinal canal is approximately  $45^{\circ}$ . For practical purposes, it is sufficient to obtain this angle with the skin, although in doing so one must consider the degree of obesity present. The feeling experienced in transversing the structures between the skin and the transversalis fascia is characteristic to the experienced touch. The first pronounced sensation is the "jump" of the needle point in going through the aponeurosis of the external oblique. This sensation varies in different patients, depending upon the degree of firmness of the fascial structure. There is a definite lack of resistance comparable with the successful entry of the spinal canal during a lumbar tap.

Having reached the plane of transversalis fascia, the syringe is depressed and the needle point carried down further in the direction of the pubic spine until the region of the internal ring is reached. With the standard 3-inch needle, starting the injection  $1\frac{1}{2}$  inches above the internal ring, the needle will penetrate about  $2\frac{1}{2}$  inches of tissue before the internal ring is reached. One should always attempt to follow the needle point in its voyage by palpation with the opposite hand. In the thin subject it is often possible to feel it throughout the entire procedure. This is aided by depressing the syringe from time to time.

The second and third injections are given in the same region (Fig. 3, 2, 3), attempting to reach the medial and lateral borders of the ring. Occasionally some of the solution will diffuse toward the internal oblique muscle to cause swelling above the canal the following day. This reaction subsides promptly, but the symptoms may cause apprehension on the part of the patient unless he is warned beforehand.

The fourth injection is started about  $\frac{3}{4}$  inch above the internal ring and the needle point carried through the external oblique aponeurosis and the muscles beneath it. Then the syringe is depressed and the needle carried through the canal to the external ring where it is palpated by the examining finger which has invaginated the scrotum. The solution is deposited as the needle is withdrawn, so that the entire canal is bathed.

With every injection, it is advisable to aspirate first to make certain that no blood vessel has been entered. Following this, a few minims of solution are injected and the resulting symptoms noted. After a lapse of three or five minutes, if no cramplike peritoneal symptoms are complained of, the remainder of the solution is slowly deposited.

The fifth, sixth, seventh, and eighth injections are made, as noted on the diagram, in the midcanal area (Fig. 3). In this region the roof is composed mainly of external oblique aponeurosis. This makes the injection a very simple procedure, the only caution to be observed being



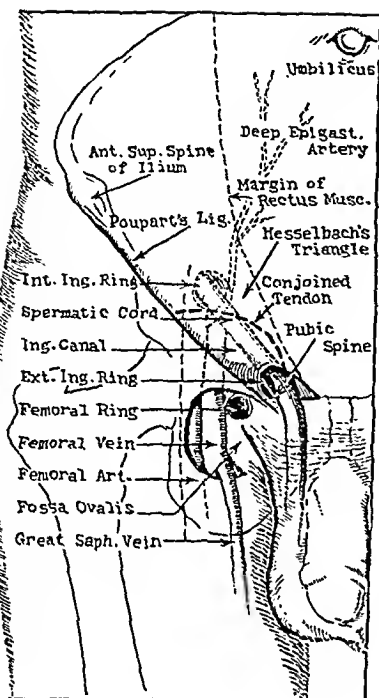


Fig. 1.

Fig. 1.—Surface markings.

Fig. 2.—Area injected in treatment of: A, indirect inguinal hernia; B, direct inguinal hernia; C, femoral hernia.

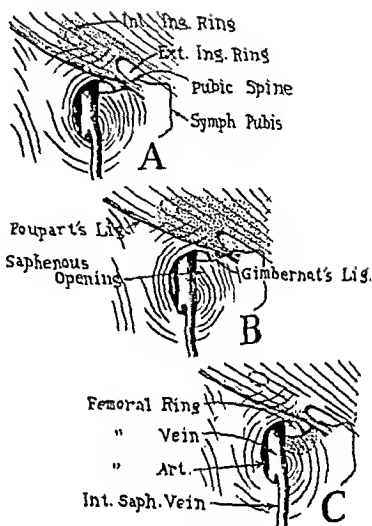


Fig. 2.

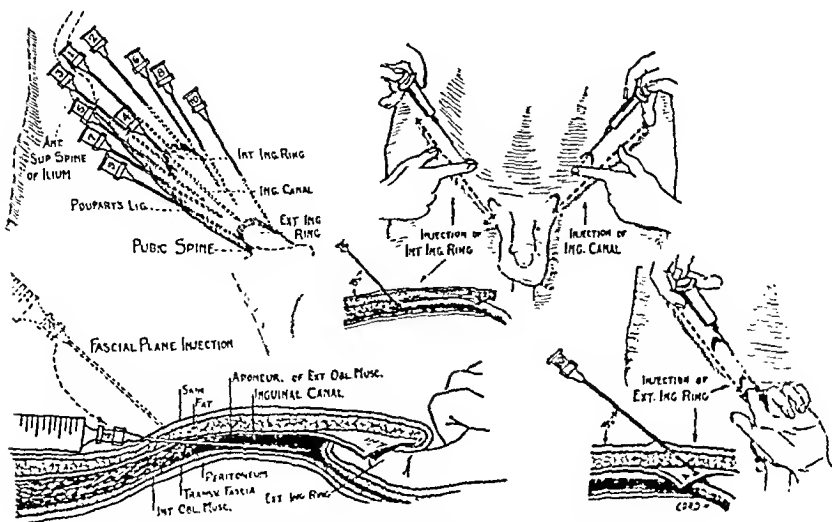


Fig. 3.—Injection of indirect inguinal hernia.

direction of the needle point, as in subsequent injections, is toward the pubic spine and the angle that the needle makes with the inguinal canal is approximately  $45^{\circ}$ . For practical purposes, it is sufficient to obtain this angle with the skin, although in doing so one must consider the degree of obesity present. The feeling experienced in transversing the structures between the skin and the transversalis fascia is characteristic to the experienced touch. The first pronounced sensation is the "jump" of the needle point in going through the aponeurosis of the external oblique. This sensation varies in different patients, depending upon the degree of firmness of the fascial structure. There is a definite lack of resistance comparable with the successful entry of the spinal canal during a lumbar tap.

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The fifth, sixth, seventh, and eighth injections are made, as noted on the diagram, in the midcanal area (Fig. 3). In this region the roof is composed mainly of external oblique aponeurosis. This makes the injection a very simple procedure, the only caution to be observed being

avoidance of the cord. With the fifth and seventh injections, Ponpart's ligament should be injected so as to favor adhesions to this important stable supporting structure.

The general angle of all the preceding injections is the same and the needle point is always carried toward the pubic spine. This makes for what may be called the angle of safety. Our cadaver work has convinced us that no other approach is as safe, and clinical experience has confirmed our observations.

The injection of the external ring is comparatively simple. For this procedure, it is always advisable to keep the examining finger in the ring itself. The crura are injected separately (ninth and tenth injections) and the needle point carried through the spermatic fascia, so that, on withdrawal of the syringe, the various layers of fascia are successively infiltrated.

No case is ever complete without a few injections in the region of the conjoined tendon as described later. This is important to avoid a direct hernia which sometimes follows and often coexists.<sup>39</sup> The total number of injections varies with each case and with the type of solution used. The average number is fifteen but no case should be considered cured unless the inguinal canal is definitely fibrotic to the touch of the needle and all hernial impulse has been obliterated.

#### DIRECT HERNIA

There is an essential anatomical difference between the two types of inguinal hernia which forms the basis for the variation between the two techniques. In the indirect hernia the posterior wall of the inguinal canal is relatively intact. In direct hernia this structure is either weak or goes into the formation of the hernial opening (Fig. 4). In view of the fact that in the latter case there is nothing in the inguinal canal itself that can be considered a safe anchorage point, it is necessary to go outside of the canal to secure firm and lasting adhesions. Following the basic principle of anchoring weak to relatively secure tissue, in this type of hernia it is necessary to form adhesions between the conjoined tendon, transversalis fascia, and the ligaments attached to the pubic bone in that immediate region. Merley obliterating the inguinal canal itself, as has been recommended by other writers, is not sufficient to close this type of defect.

The technique for the injection of the upper half of the canal is exactly the same as in the indirect type. It is advisable to dispose of these injections early in the treatment so as to be able to concentrate on the region of the conjoined tendon. However, the obliteration of the upper half of the canal should not be neglected, even though it shows no apparent weakness, in order to prevent the development of an indirect hernia following the treatment. In those cases where the type of hernia

is not clear cut, or where a saddle-bag or combined type of hernia exists, the internal ring becomes an important consideration and is attacked with more emphasis.

Ordinarily, as illustrated in Fig. 5, the routine of injections is as follows: The first to fifth injections are performed in order to obliterate the upper half of the inguinal canal as described previously. The superior crus and the layers of the spermatic fascia are next infiltrated by the bimanual method (Figs. 3, 10 and 5, 6). The cord is easily avoided. The inferior crus is then attacked. For this the invaginating finger is again used as a guide, the needle point being inserted over Poupart's ligament,  $1\frac{1}{2}$  inches lateral to the pubic spine. The layers of spermatic fascia and the aponeurosis forming the crus are infiltrated (Fig. 5, 7).

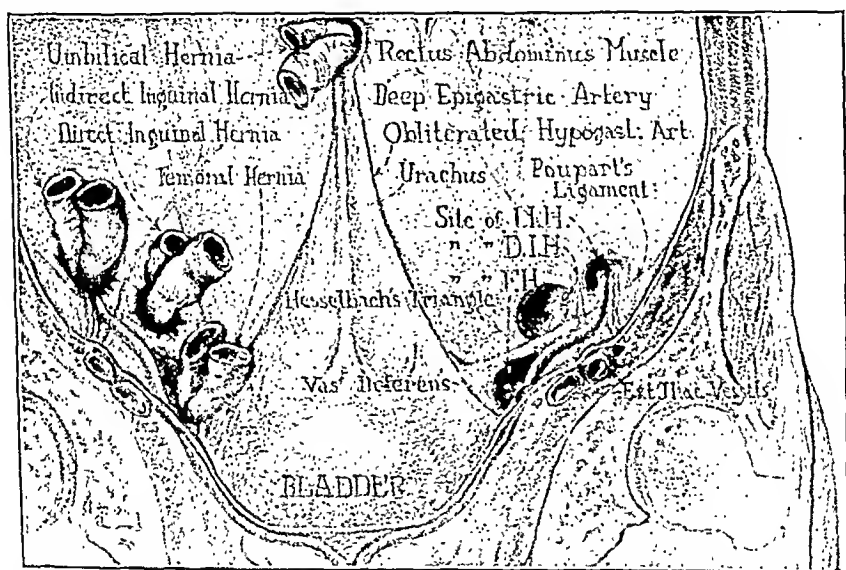


Fig. 4.—Anterior abdominal wall from within showing sites of umbilical inguinal and femoral hernias.

The important feature of the technique is the injection of the conjoined tendon. In order to perform this properly, the detailed anatomy of this structure must be known. Its condition should be ascertained at the outset of every case and one should note whether the tendon is displaced, thinned out, or not palpable. The rectus tendons must not be confused with the conjoined tendon. This is important because these two structures are attached closely together in the region of the pubic crest and pectineal line. Differential diagnosis is made by having the patient lie on his back, and, after placing the examining finger in the external ring, asking him to sit up. The opposite hand palpates the abdomen during this procedure and feels the contraction of the rectus muscles. The belly of the rectus muscle can be felt to tighten, and the muscle followed down to the tendon at its pubic insertion, where it is

also felt by the finger in the external ring. The conjoined tendon is more difficult to outline. However, in some cases, the edge is palpable. In others, the condition of the tendon itself can be made out as either firm or stretched. It is often possible to push the examining finger beyond the edge of the conjoined tendon against the transversalis fascia. In this position, the examining finger may be gripped tightly by a sphincter-like mechanism as the patient is asked to sit up.

In injecting this important structure, the needle is started at a point  $1\frac{1}{2}$  inches lateral and superior to the pubic spine, keeping the syringe parallel with the lateral border of the rectus muscle. The needle is aimed at the pubic spine. The point pierces successively the skin, superficial fascia, external oblique aponeurosis, conjoined tendon, and is arrested by the pubic spine (Fig. 5, 9). The needle is now withdrawn

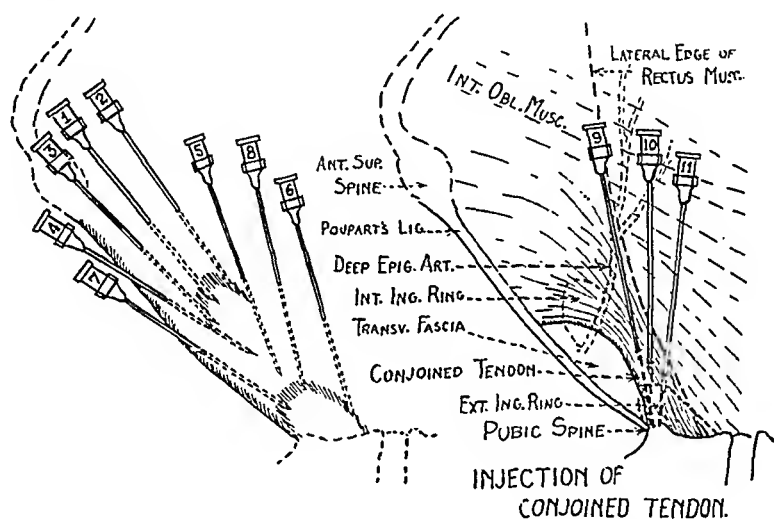


Fig. 5.—Injection of direct inguinal hernia.

slightly so that its tip does not rest upon the bone and the injection started. At this point the needle point will lie either in or below the conjoined tendon. With the bladder empty, this region is a relatively safe one for injection because of the absence of important structures. The injection is completed as the needle is slowly withdrawn. Several injections are made in that region, the fluid being distributed along the area of insertion of the conjoined tendon. By slightly varying the injection angle (Fig. 5, 10, 11) points medial and posterior to the pubic spine are infiltrated. It is important throughout this technique to make certain that one is in the safe area. If bone is not felt at the proper level, one should not inject, because it is possible to slip beneath the pubic ramus and endanger the bladder and peritoneum.

With properly performed technique, there is surprisingly little pain during this deep injection. The number of treatments given in the con-

joined tendon region vary from two to six depending upon the weakness of this structure as determined by preliminary examination. The induration following this treatment is often firmer than in the other portions of the canal, probably because of its relationship to the pubic bone. The last injections are made around the external ring itself. The crura are again infiltrated until it is certain that complete closure of the ring has taken place.

The perfect truss for hernial obliteration that can be worn comfortably day and night and in addition be waterproof has not been developed. Harris and White<sup>39</sup> have investigated this problem thoroughly and their paper describes the type of truss they recommend. Their important contribution rests on the recognition of the fact that the usual truss does not give properly directed pressure over the inguinal canal. This corresponds with our experience. It is necessary to modify the ordinary truss to make it suitable for injection therapy.

Harris and White advise the use of semirigid or rigid trusses with L-shaped extensions posteriorly pointing downwards toward the buttock. This revival of an old principle in truss construction changes the angle of pressure that the pad exerts. The fulcrum in the back of the truss directs the line of force through the inguinal canal at right angles to the truss pad. With the band of the truss properly placed midway between the crest of the ilium and the trochanter of the femur, it remains stationary and the pressure over the canal is at its maximum. We feel that the establishment of this principle is an important contribution to the problem of truss control.

Pads should be resilient and oval in shape. The truss is so adjusted that the lowest position of the pad is above the pubic crest. Thickening of the pad at one end is advisable. In indirect hernia it should be built up to exert more pressure over the internal ring. Conversely, in direct hernia, it should be thicker at the lower end.

A waterproof truss can be built on these principles. The frame may be of the semirigid type using phosphorbronze tubing. Rubber straps and pads can be added. Another arrangement is to have a leather-covered frame truss as a base and have the leather dipped in paraffin. The pads in this type may be of sponge rubber covered with paraffin-dipped leather. The usual precautions advised by previous writers must be carefully observed. In brief, the truss must be worn day and night until the completion of the treatment. We permit mild cases to sleep with an elastic truss but insist on the rigid appliance for daytime use. After completion of treatment, the patient is advised to continue the day truss for a period of three to six months, depending upon the severity of the case. Sleeping and bathing may be permitted without any truss soon after the last injection in many cases.

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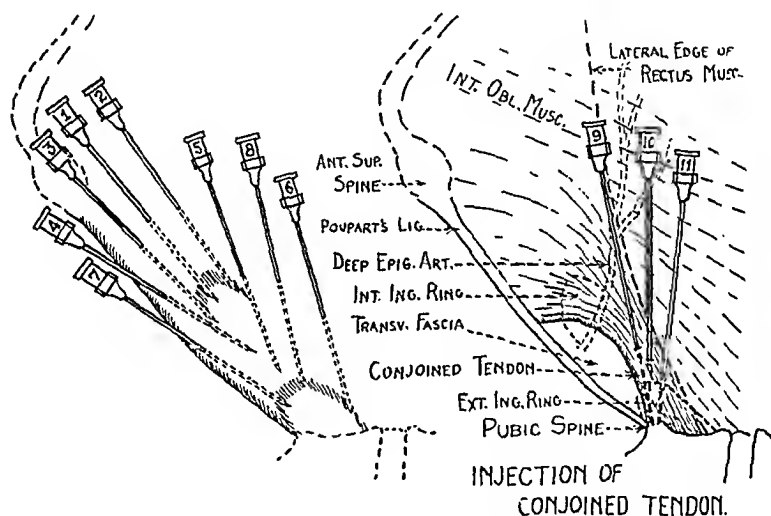


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## SUMMARY

1. The need for a safe technique in the injection treatment of hernia has been emphasized.
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7. Truss control is as important as technique.
8. Increase in safety of injection coupled with standardization of technique places this procedure on a secure foundation.

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The technique just described is based upon cadaver studies in the Anatomy Department of the New York University Medical College. This technique has been used by us on over 200 patients in the past two years. These include clinic cases at the Stuyvesant Polyclinic and the private practice of one of us (H. I. B.). Approximately 3,500 injections, therefore, have been given by this method.

While a discussion of the permanency of cure is not within the scope of this paper, it has been noted that strict adherence to the method outlined above has given more definite results than previous haphazard procedures. Furthermore, as experience with this technique increased, intraperitoneal accidents became rare and the confidence of the operator increased. In the occasional cases of early recurrence, it was possible to determine the site of weakness and to reinforce this area by additional injections. Having a standard technique of this type makes the injection treatment more controllable and productive of better results.

A number of complications were noted in our series. Intraperitoneal injection with temporary shock occurred chiefly in the beginning of the study. The symptoms resulting from this type of insult generally subsided with rest in thirty minutes. In some cases of peritoneal shock the symptoms are due only to chemical irritation of the parietal peritoneum without actual penetration of this structure. This accident can be differentiated from peritoneal entry only by the comparative mildness of the symptoms and the absence of migratory pains. The only actual danger, in our opinion, with this treatment is the perforation of gut. Fortunately, this has never happened in our experience.

Hydrocele of the testicle or cord occurred rather infrequently (five times) in this study. Occasionally small nodules developed in the region of the external ring. These were either enlarged lymphatic glands or small cystic masses, difficult to diagnose. None of these fluid collections resulted in permanent pathology. The cord itself became temporarily swollen fairly often. Other edema noted were those of the subcutaneous tissues in the region of the inguinal canal, and muscle infiltrations at the internal ring in cases where fluid had diffused through these tissues. Mention should be made of transient puffiness over the pubic region and edema of the scrotum, sometimes with adhesion to the fascia of the cord or testicle. Sterility and impotence may be dismissed because of their complete absence in our experience which coincides with that of other writers, notably Rea.<sup>35</sup>

The efficiency of this technique in cases of postoperative recurrent inguinal hernia must be mentioned before concluding. However, the outstanding fact in our experience to date has been the ease with which children and young adults respond to this technique.

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## GYNECOMASTIA

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**G**YNECOMASTIA was first reported in the literature by Basedow<sup>1</sup> in 1848. His case was associated with hyperthyroidism, as were those reported by Starr,<sup>2</sup> Freeman,<sup>3</sup> Besley,<sup>4</sup> Menville,<sup>5</sup> and Sterling.<sup>6</sup> Starr's two cases improved after thyroidectomy, one of them returning to normal with the disappearance, also, of an accompanying narcolepsy. Dey<sup>7</sup> and Ramdas<sup>8</sup> each reported a case; and in these two no additional endocrine disturbances were noted, both young men having normal sex characteristics. These cases were treated by removal of the breasts. Tellgmann<sup>9</sup> reported a case following destruction of one testicle. Lewis and Geschickter<sup>10</sup> reported ninety-five cases from the Johns Hopkins Hospital pathologic records, some of which were associated with atrophy of the testicle and imperfect development of sex organs. These authors believe there is a definite relationship between the sex organs and gynecomastia, and state that 15 per cent of the cases begin at or shortly after puberty. They also state that malignancy has not been observed, but they quote Kriss,<sup>11</sup> Bailey,<sup>12</sup> Cairns,<sup>13</sup> Heidrich,<sup>14</sup> Ferguson,<sup>15</sup> and Hertzzenberg<sup>16</sup> as emphasizing chorionepithelioma and teratoma of the testicle in relation to gynecomastia, and quote Roth<sup>17</sup> and Mochling<sup>18</sup> as reporting breast enlargement in men with hypophyseal tumors, and Mathias and Weber as describing gynecomastia in a man with a malignant tumor of the adrenal cortex. More recently Lisser<sup>19</sup> reported a case of adrenal cortical tumor in an adult male causing gynecomastia and lactation, and stated that a total of five cases had been reported in the literature, one of which, Holl's,<sup>20</sup> had survived operation, with a return to normal masculine characteristics. The others died. Lisser suggests that possibly a hormone which supports lactation, called cortilactin, is secreted in such large amount in adrenal cortical tumors as to cause the gynecomastia. Entwistle and Hepp<sup>21</sup> have had a case of testicular chorionepithelioma with pregnancy reactions, a positive Aschheim-Zondek, lactation, and pituitary changes like those in a pregnant woman. A case of unilateral gynecomastia in a 16-year-old colored boy is described by Cole and Elman.<sup>22</sup> This enlargement followed trauma to his chest. It was removed surgically. Edwards, Shimkin, and Shaver<sup>23</sup> observed the development of bilateral gynecomastia in the course of treatment of a case of Addison's disease with adrenal cortex extract. During a rest period in treatment, the breasts receded to almost normal, but increased in size when the treatments were resumed.

At necropsy this patient's adrenal glands showed primary atrophy of the cortical glands and a marked preponderance of the chromophobe cells of the pituitary gland.

This evidence would seem to indicate a relationship between gynecomastia and any or all of the glands of internal secretion, but the testicle seems most constantly associated, whether there be atrophy, chorionepithelioma, or teratoma. From the standpoint of frequency, the thyroid, adrenal, and hypophysis seem to be associated in that order. In some of the cases there were found no discernible endocrine disturbances. The etiology, therefore, is still obscure. Moszkowicz said testicular secretion inhibits growth of the male breast. Kriss states that gynecomastia is not caused by cessation of inhibitory action of the testicles on the mammary glands.

The treatment, if any, has usually been surgical. The indication for surgical treatment, except in cases of definite tumors, has been embarrassment when dressed in a swimming suit, or fear of malignancy in the breast. There is seldom any real discomfort. It was because of embarrassment and fear of malignancy in the breast that the following cases presented themselves.

#### REPORT OF CASES

CASE 1.—P. E., Jr., aged 20 years, white male of small stature and slender build, was first seen June 22, 1936. He complained of a tender, enlarged breast on the right side which dated back three and one-half years to a blow over the right nipple by a baseball. The breast began to enlarge in four months and had been of the present size for two years (Fig. 1 A). In March, 1936, he had an appendectomy, and the breast decreased in size for twenty-four hours, only to return to its enlarged size suddenly within the next twenty-four hours.

Physical examination showed a well-developed right breast the size of that of an average 15-year-old girl. It was soft and of even consistency, there being no nodules. The areola was somewhat enlarged. The left side was normal. The right testicle was normal, but the left one was about half as large as the right. The voice was masculine. Hair was sparse on the face, requiring a shave once in a week or ten days. Hair was somewhat sparse also in the axillae and at the pubis. The penis was rather small. The Aschheim-Zondek test on his urine was negative. There were no other findings of significance.

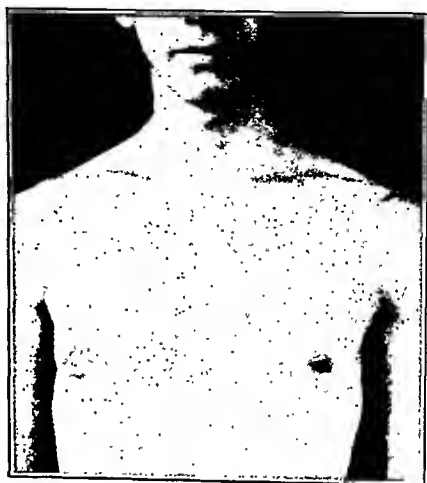
Before resorting to surgical removal of the breast, it was decided to try hormone therapy, on the theory that, if the small left testicle could be made to enlarge to normal size, the breast might recede. Beginning July 20, 1936, he was given, twice a week, an injection of anterior pituitary-like hormone, there being given a total of 10 e.e. in five divided doses. By Aug. 3, 1936, there was no noticeable change in breast or testicle, and on Sept. 28, 1936, treatment with male sex hormone, testosterone propionate,\* was begun intramuscularly. The first twenty-one doses, given twice a week, were each 2.5 mg. per dose. By Oct. 29, 1936, there was an appreciable decrease in the size of the breast and increase in the size of the left testicle. The fourteenth dose was given on Dec. 21, 1936, and at this time the left testicle was half again the size it was when testosterone treatment was instituted, but the breast had shown no further change. The patient said he had to shave oftener. On Jan.

\*The testosterone propionate used in these cases was oreton, which was kindly furnished by the Schering Corporation, Bloomfield, N. J.

25, 1937, the penis seemed larger, the breast was about one-half its original size, the left testicle seemed a little larger, and the patient was shaving three times a week. On March 15, 1937, the dosage of testosterone was increased to 5.0 mg., this being the twenty-second dose. At this time the left testicle was almost equal to the right in size, and there was little more, if any, change in the breast. After seven 5.0



A.



B.



C.

FIG. 1.—A, Case 1, showing enlarged right breast in June, 1936, before treatment. B, Case 1 in June, 1937, after having received 87.5 mg. of testosterone propionate in twenty-eight divided doses. Treatment was continued with 25.0 mg. doses until a total of 162.5 mg. had been given without further change. The breast has decreased markedly in size, but it is still larger than the unaffected side. C, Case 1 in July, 1938, showing recurrence of one month's standing. He had received no treatment for ten months but, since the photograph was taken, testosterone propionate have been resumed. However, over a period of three weeks, 165.0 mg. of testosterone propionate have been given without effect.

mg. doses had failed to produce further improvement, the dose was increased to 25.0 mg. each on June 28, 1937. A photograph was taken at this stage (Fig. 1 B) which was just a year from the time the patient was first seen, and after he was given a total of twenty-eight injections. At this time the left testicle had increased to almost the size of the right, and the breast had decreased to less than one-third its size when first seen. The hair on his face had become heavier, and he was shaving every other day. Libido was increased. Treatment with 25.0 mg. doses was continued irregularly until Sept. 23, 1937, without apparently any further change, and discontinued with the forty-third dose on that date. The patient felt no more embarrassment, was more decidedly masculine in character, and was pleased with the result.

On July 11, 1938, the patient returned to the clinic. His right breast was fully as large as it was when he first was seen on June 22, 1936. His left testicle was apparently as small as it was at that time and measured  $1\frac{3}{16}$  by  $\frac{3}{4}$  by  $1\frac{5}{16}$  inches. The right testicle measured  $1\frac{7}{16}$  by  $1\frac{3}{16}$  by 1 inches. A photograph (Fig. 1 C) of



Fig. 2.—Case 2, in whom there was no change after prolonged treatment with large doses of testosterone propionate. He has also received anterior pituitary substance without effect. This patient is five years older than the patient in Case 1.

the breast at this time shows it to be almost identical in appearance with that of the first photograph (Fig. 1 A), taken before treatment was started in June, 1936. This recurrence was noticed only five weeks before the patient reported on July 11, 1938, and developed rapidly to its present size without history of trauma. Treatment with testosterone propionate was started with 10.0 mg. doses three times a week, and, after the fourth dose, it was increased to 25.0 mg. three times a week. By Aug. 1, 1938, he had had 165.0 mg. in three weeks without any apparent change in the breast. The atrophied testicle, however, had enlarged slightly, measuring  $1\frac{5}{16}$  by  $\frac{5}{8}$  by 1 inches. Libido was increasing rapidly, and hair on the face was again growing faster. Testosterone propionate, 25.0 mg. per dose, is being continued three times a week.

CASE 2.—J. A., Jr., aged 24 years, a white male of average height, but slender, first seen at the clinic on July 25, 1936, complained of an enlargement of his left breast. Five years previously he was struck over his left chest with a bundle of books. The left breast became enlarged and remained the same size to date. He sought advice because of fear of malignancy, rather than from embarrassment. He is married and the father of two children.

Physical examination revealed a somewhat enlarged breast on the left side (Fig. 2) which was slightly tender on palpation, but not painful. The nipple was not much larger than the right. There were no hard nodules present, but some glandular tissue was palpable. This breast was not as large as that in the previous case. The testicles were equal in size. The Aschheim-Zondek test was negative. The thyroid was palpable, and the basal metabolic rate was plus 16. There were no signs of hyperthyroidism, and physical findings were otherwise negative.

Treatment with testosterone propionate was started on Nov. 8, 1936. Injections were given twice a week. There were rest periods from one to three weeks scattered throughout the course. The first twelve doses were 2.5 mg. each, the next ten were 5.0 mg. each, and from the twenty-third through the fifty-first the dose of each injection was 25.0 mg. The last injection was given on Sept. 1, 1937, when treatment was discontinued because there was no appreciable change in the size of the breast. This patient had received eight more injections, and more concentrated dosage, than the preceding one, without a favorable result. During June and July, 1938, this patient received anterior pituitary substance intramuscularly two or three times a week without effect. The breast is unchanged.

CASE 3.—M., aged 24 years, a single white male of average height and quite well built, was seen once only, on March 5, 1938. He had a right breast similar to that described in Case 1. At the age of 16 years he received a blow on the right chest while boxing. The breast immediately became swollen and tender, and gradually increased in size during the next two years, since which time it has been unchanged. Libido was normal.

Examination revealed a well-developed right breast, with a slightly enlarged nipple and areola. There were a few small firm nodules present, and they were quite tender on palpation. The glandular structure was easily felt. There was no secretion. The left testicle, which the patient thought was the larger, was in fact smaller than the right. There was a moderate varicocele on the left side. He was otherwise normal and decidedly masculine.

Photographs, laboratory work, and treatment were not possible in this case, as the patient did not return. Certain points are of interest for comparison with the two previous cases and will be discussed later.

CASE 4.—E. McC., aged 16 years, colored, well developed for his age, came to the clinic on April 18, 1938, because of double breast enlargement which had been present two years. He associated this enlargement with a fall across the handlebars of his bicycle, wherein both sides of his chest were injured. He gave a history of having had an undescended testicle on the left side. At the age of 9 years, when seen in the dispensary, the left testicle was still undescended. The testicle is now in the scrotum, but the patient is not sure about the time of its descent. Two years ago he was operated upon for a right inguinal hernia. He is in the eighth grade in school and ascribes his apparently slow progress to having been out of school at different times, claiming that he has no difficulty in keeping up with the other students in his classes. When first seen, the patient gave a history of not having had an erection or any other signs of libido.

Physical examination revealed a strong looking boy in good physical condition. He seemed to be of average intelligence. Both breasts were enlarged and dome-shaped, with the left being slightly larger than the right. The nipples and areolae were swollen and enlarged to twice the normal size. Glandular tissue was palpable in the breasts, but there were no hard nodules. They were very slightly tender on palpation. Both testicles were in the scrotum, but the left was about two-thirds as large as the right. The penis was normal in size. The Aschheim-Zondek test of his urine was negative. His basal metabolic rate was minus twelve. There were no other findings of note.



Treatment with testosterone propionate was started on May 11, 1938. The initial dose was 25.0 mg. and was given intramuscularly. The treatments were given approximately three times a week. On May 22, 1938, when he received his sixth injection, his breasts were definitely smaller. On June 6, 1938, when he received his tenth injection, both breasts showed a marked decrease in size. At this time the atrophied left testicle was almost as large as the right, there was more pubic hair,



Fig. 3.—Front, A, and side views, B, of Case 4, who is 16 years of age, before treatment.



Fig. 4.—Front, A, and side views, B, of Case 4 after having received a total of 320 mg. of testosterone propionate in the course of two months. A definite reduction in size of the breasts will be noted.

and he seemed to act a little livelier. Libido was still absent. On June 13, 1938, his breasts were practically flat, the nipples were normal in appearance, and his testicles were very nearly equal in size. At this time he had received a total of 300 mg. of testosterone propionate, in twelve doses. Because the breasts and testicle seemed to have been brought back to normal, the dose of each injection was reduced to 10.0 mg. and continued three times a week to determine what effect, if any, these additional

treatments might have on libido. On June 27, 1938, the patient stated he had had his first erection a few days previously. By July 18, 1938, he had received a total of 405.0 mg. of testosterone propionate in a little over two months. Libido had been decidedly increased, the penis was much larger, and calibration of his testicles showed the right to measure  $1\frac{1}{8}$  by 1 by  $1\frac{1}{16}$  inches and the left  $1\frac{3}{16}$  by  $1\frac{1}{16}$  by  $\frac{7}{8}$  inches. On Aug. 1, 1938, the left testicle measured  $1\frac{1}{2}$  by  $1\frac{1}{8}$  by  $\frac{7}{8}$  inches, and the penis was still larger than at the time of the examination a week previous. Treatments are to be continued if necessary once a month or oftener to maintain the present favorable result. Figs. 3 *A* and *B* show front and side views of this patient before any treatment was given. Figs. 4 *A* and *B* show corresponding views after 320 mg. of testosterone propionate had been given in fourteen doses.

#### COMMENT

Four cases of gynecomastia herein reported have certain similar characteristics. All but Case 4 were unilateral. All gave a history of trauma. All occurred while the patients were in their "teens." No one of them showed any evidence of disturbance in any of the glands of internal secretion except the testicles, and all but Case 2 had an atrophied left testicle. The Aschheim-Zondek test was negative in the three that were given treatment. The other (Case 3) was not examined, for reasons previously given. Libido was increased in two of the three treated cases and was very much present in Case 3, who was not treated.

These cases are among the first observed with testosterone therapy. Bronstein<sup>24</sup> reported a case of the less frequent bilateral type treated with androsterone and testosterone propionate. His patient was a 17-year-old colored boy with atrophied testicles, a positive Friedman test, no libido, no secretion from the breasts, and a rather effeminate personality. After treatment with androsterone, and later testosterone propionate, he noted the following suggestive changes: (1) Appearance of erections, and hair on the face, chest, and legs; (2) noticeable interest in the opposite sex; (3) questionable enlargement of testes and shrinkage of right breast.

A case of unilateral (left-sided) gynecomastia in a boy 14 years of age is now being treated with testosterone propionate by Birnberg, Kurzrok, and Livingston.<sup>25</sup> They report "the breast has become considerably smaller, but the patient is still under treatment." They are giving 10.0 mg. of testosterone propionate twice a week.

Wolf<sup>26</sup> advises that injection of androtin and anterior pituitary-like substance generally results in a decrease in the size of the breast. He recommends pituitary and adrenocortical hormone substance to stimulate testicular development if there is merely hypofunction of the testicles. If Case 2 were merely one of testicular hypofunction, for the testicles were equal in size, it might have been expected that testosterone would stimulate them enough to cause at least some change in the breast, but it had no apparent effect. Nor has anterior pituitary substance had any effect in this patient after two months' treatment.

The favorable results obtained in Cases 1 and 4, as opposed to the unfavorable result in Case 2, in spite of the fact that they all received practically the same treatment, may be due to two factors. In Cases 1 and 4, which responded to treatment, there was marked atrophy of the left testicle, while in Case 2 the testicles were equal in size and apparently normal. In Cases 1 and 4 the breast enlargement occurred earlier after puberty (at 16 and 14 years respectively) than Case 2 who was 19 years of age when his breast enlarged. Cases 1 and 4 were also considerably younger than Case 2 when endocrine therapy was given. Case 4, whose breasts enlarged at 14 and whose treatment was given at 16, responded more quickly than Case 1, whose breast enlarged at 16 and received treatment at 20. Age, therefore, may be an important factor. In view of our meager experience a good prognosis with hormone therapy would appear to be dependent upon the development of gynecomastia soon after puberty, and likewise upon the institution of treatment at an early age. Testicular atrophy seems to be definitely associated in a large percentage of cases, particularly so far as the efficiency of testosterone therapy is concerned.

The favorable outcome in two out of three cases of gynecomastia treated with testosterone propionate suggests that in cases of this kind endocrine therapy should be given a thorough trial before surgical removal of the breast is advised. The spontaneous recurrence of the right breast in Case 1, associated with recurring atrophy of the left testicle, suggests that probably replacement therapy with male sex hormone at regular intervals will be found necessary to maintain a cure once it has been effected.

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## THE REMOVAL OF BENIGN TUMORS OF THE BREAST WITHOUT VISIBLE SCARS

W. WAYNE BANCOCK, M.D., PHILADELPHIA, PA.

*(From the Surgical Department of Temple University)*

TO THE person of aesthetic sense, a disfiguring scar engenders an inferiority complex, continuously activated by the physical deformity. To a sensitive woman scars upon exposed portions of the body and breasts are especially objectionable. In the past incisions radiating from the nipple which leave such scars have commonly been employed for the drainage of abscesses and the excision of benign tumors. But the skin overlying the mammary gland is very elastic and, aided by the underlying loose fascia, nearly any portion of the gland may be brought near the margin of the areola for excision. Aseptic incisions along the areolar margin, accurately closed, heal with an imperceptible scar, in marked contrast with the ugly disfigurement seen after incisions elsewhere. The common blue dome cysts of the breast forming well-rounded, tense masses from the size of a pea to that of a large marble may give the sensation of a solid tumor, but as a rule they are more perfect spheres or ovals. They may readily be aspirated through a rather fine hypodermic needle, and the remaining sac is so thin that no perceptible thickening remains. As these cysts, which may be multiple, seem to have no malignant tendencies, we have for years treated them by aspiration. Apparently none of those aspirated have refilled. Of course, if the needle indicates that a solid tumor has been entered, or if residual thickening remains, then exploration and biopsy are indicated.

For the removal of benign tumors, a curved incision along that part of the areolar border nearest the tumor is made. The fascia close to the gland is incised and opened by introducing and separating the blades of a Mayo scissors. Using long narrow retractors, the tissue separation or division is continued until the tumor is reached and grasped with a tenaculum or viscera forceps, and, aided by retraction, pulled into view. By dull or sharp dissection the tumor is enucleated, bleeding points being at once ligated before the tissues have retracted from view. Obliteration of the cavity left after removal of the tumor by the use of sutures is rarely necessary or desirable and may cause distortion of the breast. Even multiple tumors, lying along the periphery of the mammary gland, may be removed through the areolar incision.

If the tumor is too large to be delivered through the stretched areolar incision, it may be removed by morecellation or through an incision along the thoracomammary sulcus, where the scar will be

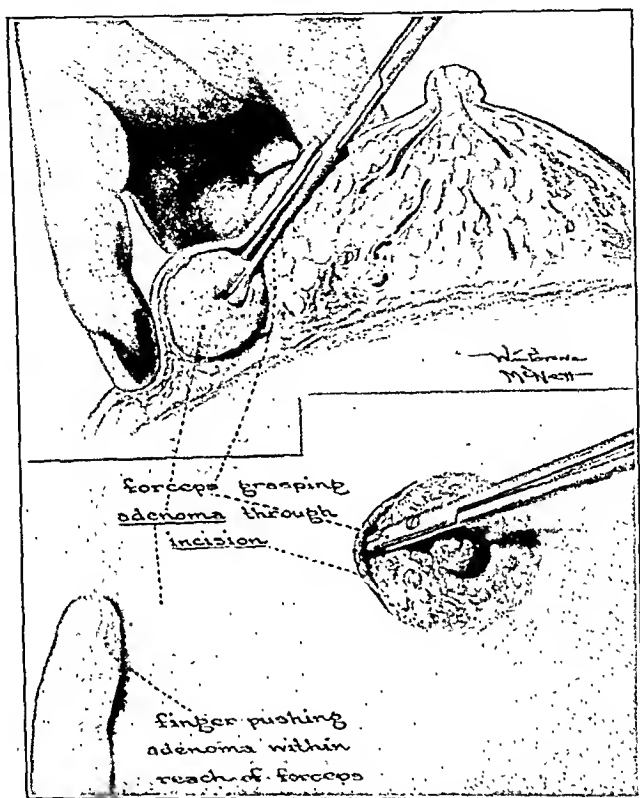


Fig. 1.—The removal of benign tumors of the breast without visible scar. A crescentic incision is made along the areolar border on the side toward the tumor. The deep fascia is tunneled by blunt dissection to the site of the tumor. Aided by narrow retractors and palpation, the tumor is grasped by forceps, brought into view, and enucleated. Each bleeding point is ligated before the retracted tissues are released. Finally, the areolar wound is closed with fine interrupted dermal sutures.

hidden by the overhanging breast. The latter incision is, of course, the best approach to all deep abscesses of the gland. Fine silk which causes less tissue reaction than catgut is preferred for ligatures in the aseptic wound, and very fine (36 gauge) alloy steel wire for the interrupted sutures to approximate the skin margins.

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cyanosis almost disappeared. The pulse rate dropped to 130, and the systolic blood pressure rose to 105. The mediastinum shifted to its normal position. The patient was placed in an oxygen tent, and 12 liters of oxygen per minute were administered.

Thirty minutes later she suddenly became quite dyspneic, lapsed into unconsciousness, became extremely cyanotic, and the pulse was almost imperceptible. Shallow respirations occurred about three or four times per minute. A silver cannula, such as that devised by Bigger,<sup>1</sup> was placed through the third right intercostal space into the pleural cavity, and several liters of air escaped under pressure. The cannula was strapped in place and covered with a rubber dam, allowing the egress but not the ingress of air. Respirations increased to 50 or 60 per minute. The pulse became palpable, and consciousness was regained. A transfusion of 500 c.c. of whole blood was given. At this time roentgenoscopic examination of the thorax, using a portable apparatus, showed bilateral pneumothorax, more marked on the left side.

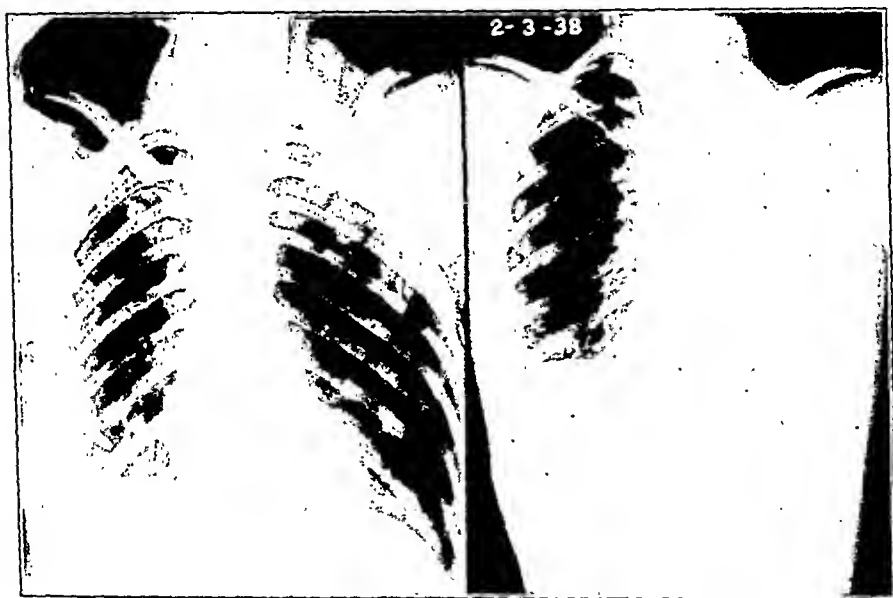


Fig. 1.

Fig. 2.

Fig. 1.—Roentgenogram showing bilateral pneumothorax and emphysema of the tissues of the neck; silver cannula is in place on the right side.

Fig. 2.—Roentgenogram showing complete atelectasis of the left lung at the time of dismissal.

Because of the relatively rapid respiration, repetition of the aspiration of the left thorax was deemed advisable and, accordingly, 950 c.c. of air were withdrawn. The initial pressure was plus 1, and the final pressure minus 11. About three hours later 300 c.c. of air were again removed from the left thorax. At 1:30 on the morning of Jan. 2 it was necessary to transfer the cannula on the right side to the region of the axilla because of emphysema and edema at its previous location. Fourteen hundred c.c. of air were again aspirated from the left side of the thorax.

The patient's condition gradually improved until the morning of Jan. 4, when the mediastinum suddenly shifted to the left side and the respiratory distress increased markedly. On physical examination complete atelectasis of the left lung seemed to be present. Bronchoscopy was considered, but it was thought best to treat the patient expectantly. Cough was encouraged, and expectoration of a consider-



# NONFATAL RUPTURE OF THE LEFT MAIN BRONCHUS FROM EXTERNAL TRAUMA

## REPORT OF CASE

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THE infrequency of rupture of a bronchus from external trauma and the rarity of recovery from an injury of this type prompt our presentation of the following case.

### CASE REPORT

A white woman, 22 years of age, was admitted to Memorial Hospital the afternoon of Jan. 1, 1938, a few minutes after she had been involved in an automobile accident. She had been unconscious for a few moments immediately after the accident. On regaining consciousness, moderate dyspnea and substernal pain were noted. Dyspnea increased and at the time of admission to hospital she was orthopneic, but rational, apprehensive, and complaining of difficulty in inspiration. There was a small laceration over the left eye and moderate subcutaneous emphysema of the neck, face, the wall of the thorax, and over the shoulders. The pulse rate was 118 and of fair volume. Respirations were 32, shallow, and labored. The systolic blood pressure was 120 and the diastolic 80.

Physical examination of the thorax revealed bilateral limitation of respiratory excursion with a tympanitic percussion note over both sides anteriorly. The breath sounds and percussion note were altered by subcutaneous emphysema, but the mediastinum was thought to be displaced toward the left side. Contusions were present over the sternum. A diagnosis was made of rupture of both lungs with bilateral tension pneumothorax.

The subcutaneous emphysema increased rapidly and within five minutes after the patient was seen, the shoulders, neck, and face were three or four times their normal size. Air was felt in the tissues over the lower abdomen, over the shoulders and arms to the wrists, and almost to the hair line of the scalp. Dyspnea became much more pronounced and it seemed that respiration would soon cease. The systolic blood pressure dropped to 60, the pulse became thready with a rate over 180, and marked cyanosis was noted. The patient became unconscious and appeared to be in extremis.

A short incision was made in the suprasternal notch, and the tissue was dissected behind the upper manubrium. Large quantities of air escaped from the wound. A small needle cannula was inserted into the intercostal space on the left side outside the nipple line, and about 700 c.c. of air were withdrawn from the thorax by reversing elevation of the bottles of the pneumothorax apparatus. The initial pressure on the left side was plus 2 c.c. of water; the final pressure, minus 4. The same procedure was employed on the right side with the aspiration of 7,000 c.c. of air; the initial pressure was plus 4 and the final pressure minus 3.

Following aspiration of air from both sides of the thorax and the employment of artificial respiration, the patient began to breathe, regained consciousness, and

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able amount of mucopurulent secretion was followed by gradual improvement. The intercostal cannula was removed from the right side on Jan. 5, and from that time the patient's improvement progressed rapidly. The ribs seemed to be intact, but a film taken Jan. 12 showed transverse fracture of the first rib on the right side, located 1 inch from the costochondral junction.

The patient was discharged from hospital Jan. 14, at which time the left lung was totally atelectatic. The right lung was apparently normal. Re-examination on Feb. 3 showed that the atelectasis of the left lung had not changed. During the interval between dismissal and re-examination she had been in relatively good condition except for slight dyspnea on exertion and a moderate cough productive of mucoid secretion. Bronchoscopic examination was recommended to determine the cause of the atelectasis.

Bronchoscopy revealed a longitudinal area of necrosis on the posterior wall of the left main bronchus, beginning at the junction of the bronchus and trachea and extending  $1\frac{1}{2}$  inches to a healing bronchial stricture. The lumen of the stricture was about 2 mm. in diameter. No secretion was present. It was deemed inadvisable to attempt to introduce dilating forceps into the stricture because of the acuteness of the reaction surrounding the lesion. The condition observed at bronchoscopy was considered representative of partial rupture of the bronchus with healing and formation of stricture.

The patient has been observed at monthly intervals and when last seen, five months after the accident, she was quite well and able to carry on her duties as a secretary.

#### COMMENT

In 1912, Schönberg<sup>7</sup> collected fifteen cases of fatal rupture of a bronchus in which compression of the thorax was the etiologic factor. In four of these cases no evidence of skeletal fracture was apparent. King,<sup>2</sup> Mumford,<sup>5</sup> and Thomas<sup>8</sup> each reported similar cases without skeletal fracture. In 1928, Krinitzki<sup>3</sup> reported the only case of recovery from this type of lesion. Rupture of a bronchus was not recognized at the time of the accident, but was discovered at post-mortem examination twenty-three years later. Meade and Graham<sup>4</sup> in 1930 summarized the previously reported cases and added one of their own, which was diagnosed at post-mortem examination, death having occurred sixteen hours after the accident. In discussing thoracic readjustment following total and partial pneumonectomy, Rienhoff<sup>6</sup> reported two patients with post-traumatic atrophy of the left lung, who were operated on for release of extrapericardial adhesions. The initial injury was not described. In both instances a crushing injury of the thorax in early childhood was apparently the etiologic factor.

From a review of the literature it would seem that the case we are reporting is unique in that the patient has recovered from the accident and the lesion has been identified during life. It is possible, of course, that infection may occur in the lung distal to the stricture, but to attempt bronchoscopic dilatation of the stricture does not seem wise at this time. If infection should occur, pneumonectomy may be indicated.

marginal vein of the ear or by cardiac puncture at stated intervals. Concentrations of both free and acetylated sulfanilamide were determined on oxalated whole blood by the method of Marshall and others.<sup>2</sup>

## PRESENTATION OF DATA

In Chart 1 are shown graphically the concentrations in the blood of free, acetylated, and total sulfanilamide following an intravenous injection of 0.75 gm. sulfanilamide in the normal rabbit under ether

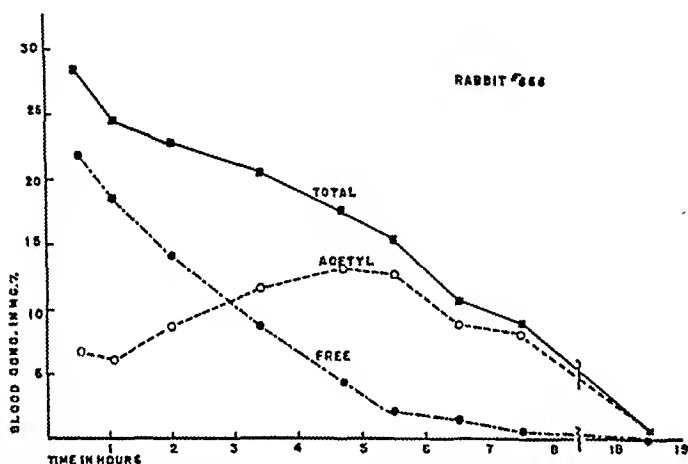


Chart 1.—Blood concentrations of total, free, and acetylated sulfanilamide in the normal rabbit after intravenous injection of 0.75 gm. sulfanilamide.

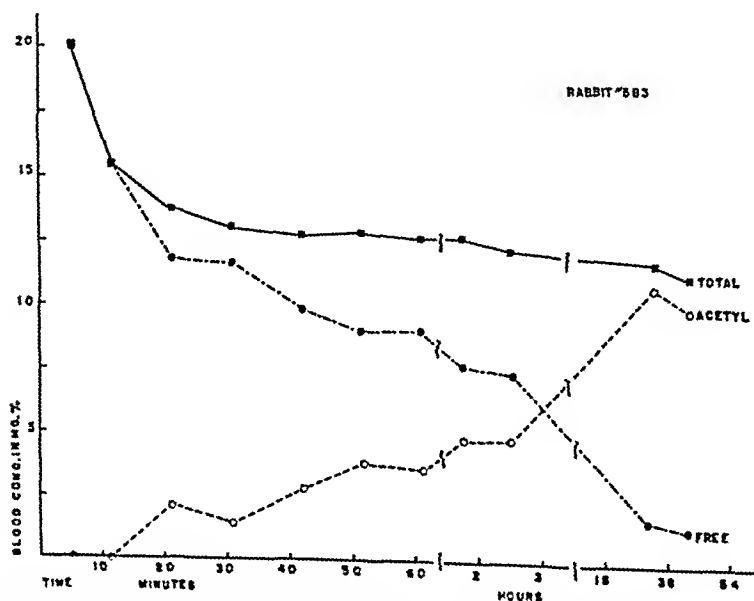


Chart 2.—Blood concentrations of total, free, and acetylated sulfanilamide after intravenous injection of 0.75 gm. sulfanilamide in the bilaterally nephrectomized rabbit.

## ACETYLATION OF SULFANILAMIDE

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THE conjugation of certain benzene ring compounds containing the amine radical has been observed repeatedly in various species.<sup>1</sup> The acetylation of another such compound, para-amino-benzene sulfonamide, or sulfanilamide, has been demonstrated by Marshall and his co-workers<sup>2</sup> in certain species, including man and the rabbit. The acetylated form of the drug becomes widely distributed in the body tissues and appears in the blood and urine. The site of the process of acetylation has been a matter of speculation, although the recent in vitro experiments of Harris and Klein<sup>3</sup> implicate the liver. The present report concerns itself with a study of the acetylation of this drug in the rabbit.

### PLAN OF EXPERIMENT

In order to determine the site of acetylation, surgical extirpation of one or more of the organs in question was performed, after which sulfanilamide was given by vein. The concentrations of free and acetylated sulfanilamide in the blood were determined at intervals subsequently. Rabbits weighing 1.5 to 2.5 kg. were used. They were divided into four groups, each group containing at least four animals. Group 1 constituted normal controls. The second group consisted of bilaterally nephrectomized animals. In the third group the gastrointestinal tract from gastric cardia to the rectum was excised, along with the pancreas and the spleen. In Group 4 total hepatectomy was performed, after first removing the gastrointestinal tract, the spleen, and the pancreas. In this group also there was one animal in which only subtotal hepatectomy was done.

The operations were all performed in one stage under ether anesthesia with a minimum of trauma. The animals were given 10 to 20 c.c. of 2.5 per cent glucose in 0.9 per cent sodium chloride solution by vein immediately after the operations. Precautions were taken against loss of body heat during and after operation. Standard doses of 0.75 gm. of sulfanilamide, dissolved in 20 to 30 c.c. of warmed water or 0.9 per cent sodium chloride solution, were given intravenously from one to three hours after operation. Blood samples were taken from the

TABLE II

BLOOD CONCENTRATIONS AFTER INTRAVENOUS INJECTION OF SULFANILAMIDE (RABBITS 101, 574, 523, 557, 589, 591 PREVIOUSLY SUBJECTED TO REMOVAL OF LIVER, GASTRO-INTESTINAL TRACT, SPLEEN, AND PANCREAS; RABBIT 465 PREVIOUSLY SUBJECTED TO SUBTOTAL HEPATECTOMY)

RABBIT NUMBER	PERCENTAGE OF LIVER REMOVED	FREE SULFANILAMIDE	ACETYLATED SULFANILAMIDE	TOTAL SULFANILAMIDE	PERCENTAGE ACETYLATED	TIME AFTER ADMINISTRATION
	%	mg. %	mg. %	mg. %	%	hr.
465	94	13.4	0	13.4	0	2.2
		13.5	0	13.5	0	3.0
		13.3	1.2	14.5	8.3	4.5
		13.0	1.1	14.1	7.8	5.5
101	100	9.0	0	9.0	0	3.0
574	100	6.4	0	6.4	0	2.0
		5.9	0	5.9	0	3.0
523	100	17.0	0	17.0	0	2.2
		16.8	0	16.8	0	4.0
		16.9	0	16.9	0	5.5
		15.5	0	15.5	0	6.2
557	100	4.0	0	4.0	0	2.0
		3.9	0	3.9	0	3.7
		4.2	0	4.2	0	4.8
		3.9	0	3.9	0	5.8
589	100	20.0	0	20.0	0	2.5
		18.0	0	18.0	0	3.6
		16.0	0	16.0	0	5.3
591	100	14.0	0	14.0	0	1.5
		14.0	0	14.0	0	2.7
		13.0	0	13.0	0	4.5
		11.5	0	11.5	0	5.4
		11.0	0	11.0	0	6.2

steady through absence of excretion, all the blood sulfanilamide soon becomes acetylated. Acetylation, then, seems to be a unidirectional process, dependent upon time rather than concentration of free sulfanilamide in the blood. This is perhaps an important consideration in the clinical use of the drug, for there is some reason to believe that acetylated sulfanilamide is less bacteriostatic than is the free form.<sup>4</sup>

Concerning the locus of acetylation, the evidence from these experiments is clear. In Table I it is seen that acetylation proceeds rapidly in the rabbit deprived of gastrointestinal tract, spleen, and pancreas, and in one such preparation, Experiment 571, the process is 84 per cent complete at the end of 3.5 hours. As pointed out above, acetylation occurs at a normal rate in the nephrectomized animal. Attention is thus focused on the liver. In the rabbit it is impossible to remove all the liver in one operation without the rapid onset of prostration and death from portal stasis. However, it is possible to remove all but the small caudate lobe closely adherent to the portal vein, comprising about 10 per cent of the liver substance, and have the animal survive from

anesthesia. The results are to be compared with data obtained in similar manner from a bilaterally nephrectomized rabbit, as shown in Chart 2. The data shown in Charts 1 and 2 are typical of the findings in the two groups. In Table I are presented data obtained in a study of six rabbits after removal of the gastrointestinal tract, spleen, and pancreas. Table II shows the results obtained in six experiments, includ-

TABLE I

BLOOD CONCENTRATIONS OF SULFANILAMIDE AFTER INTRAVENOUS INJECTION OF FREE SULFANILAMIDE IN RABBITS SUBJECTED TO GASTROENTERECTOMY, SPLENECTOMY, AND PANCREATECTOMY

RABBIT NUMBER	FREE SULFANIL- AMIDE mg. %	ACETYLATED SULFA- NILAMIDE mg. %	TOTAL SULFA- NILAMIDE mg. %	PERCENTAGE ACETYLATED %	TIME AFTER ADMINIS- TRATION hr.
571	3.7	19.5	23.2	84.2	3.5
	2.1	15.2	17.2	87.8	6.0
570	8.3	2.7	11.1	24.3	2.5
	10.6	7.9	18.5	42.7	8.0
572	8.5	4.0	12.5	32.0	2.0
	8.7	4.6	13.3	34.5	3.0
573	9.3	2.5	11.8	21.3	1.9
	9.8	3.8	13.6	27.8	2.9
574	10.1	2.2	12.3	17.8	2.5
575	9.3	4.5	13.8	32.6	2.5

ing one in which 94 per cent of the liver tissue was removed without fatal impairment of the portal circulation. In the other five experiments total hepatectomy with removal of the gastrointestinal tract, spleen, and pancreas was performed.

#### DISCUSSION

These experiments are open to the criticism to which all extirpation studies are liable; namely, the removal of an organ may disturb interlocking mechanisms and produce effects in the functioning of related viscera which confuse the picture. To this consideration must be added the uncertain effects of recent trauma, even though minimized by gentle surgical technique, careful hemostasis, and avoidance of heat loss. The acetylating process, however, seems to be carried on as a fundamental part of cell behavior, as attested by the uniformity of our results under varying conditions, and as seen in the *in vitro* experiments of Harris and Klein on liver slices.

When sulfanilamide is given intravenously in the normal rabbit, acetylation takes place with striking rapidity. As seen in Chart 1, 25 per cent of the total blood sulfanilamide is in the acetylated form, even as early as one-half hour after the injection. Chart 1 also illustrates the fact that the proportion of acetylated sulfanilamide in the blood rapidly increases, while the free sulfanilamide decreases. In the nephrectomized rabbit, as shown in Chart 2, where the concentration remains

# THE ORGANIZATION AND TECHNIQUE OF THE BLOOD BANK AT THE PHILADELPHIA GENERAL HOSPITAL

## EXPERIENCES WITH 1,000 TRANSFUSIONS

CHARLES S. CAMERON, M.D., AND L. KRAEER FERGUSON, M.D.,  
PHILADELPHIA, PA.

*(From the Philadelphia General Hospital)*

### INTRODUCTION

EARLY in 1937 the administrative staff at the Philadelphia General Hospital decided to investigate and standardize the procedure of blood transfusion. For this purpose, a committee of the surgical staff was appointed to work with the chief surgical resident. The use of conserved, defibrinated cadaver blood had been considered and given a brief trial, but it was decided to adopt the citrate method of transfusion as the standard method of the hospital, since this offered a technical simplicity over the somewhat exacting and more elaborate direct methods. Moreover, there were no clinical disadvantages apparent in a large experience with its use.

Regardless of the method of transfusion, the selection of a donor had previously been a time-consuming and labor-wasting effort. The reasons for this are as follows: (1) For every patient needing a transfusion, a number of donors must be called to the hospital to be typed, in the hope that one of them will be in the desired blood group. (2) Serodiagnostic tests must be done on the blood of every donor, requiring a trained technician to be on call at all times, unless, as in the case of emergency night transfusions, the hospital is willing to adopt the alternative of having the recipient sign a statement releasing the hospital of responsibility in the event of the transmission of blood-borne disease. (3) The above procedures, in addition to interrupting the routine of the laboratory, delay the actual transfusion, often to the point of jeopardizing the patient's life. (4) Interns on clinical services already busy must interrupt their work to draw samples of blood from the prospective donors and later to collect blood from the donor selected. This often makes a considerable interruption in the ward routine if several donors for two or three patients come in at the same time. They usually are anxious to see the patient and oftentimes they are unwilling to wait while the typing and Wassermann tests are being performed.

These objectionable features have been eliminated at the Philadelphia General Hospital through the establishment of a central repository or blood bank for citrated blood as was suggested by Fantus.<sup>1</sup> We have



12 to 24 hours. In such preparations, as shown in Table II, acetylation occurs, but at a greatly reduced rate. In Experiment 465, in which the animal was deprived of 94 per cent of the liver, the blood at the end of 5.5 hours contained about 8 per cent of the total sulfanilamide in the acetylated form. Other experiments, not described here, show that after 80 to 90 per cent of the liver tissue is ablated the rate of acetylation falls off sharply. On considering the responses of the totally hepatectomized rabbits, subjected also to gastroenterectomy, splenectomy, and pancreatectomy, we find that these animals in no case show power to acetylate, even though the survival period is 18 to 24 hours. Thus it seems clear that acetylation of sulfanilamide does not occur in the absence of the liver.

In Chart 2, which shows data typical of the findings in nephrectomized animals, one sees confirmation of the conclusion of Marshall and others<sup>2</sup> and of Stewart, Rourke, and Allen<sup>5</sup> that sulfanilamide is excreted only through the kidneys. The ready diffusibility of the drug also is demonstrated, for within 30 minutes after the intravenous injection was made a steady total sulfanilamide concentration has been reached. The stability of this level suggests that the acetylated molecule is also highly diffusible, and that it likewise enters the body fluid mass freely.

#### CONCLUSIONS

1. The liver is the site of acetylation of sulfanilamide in the rabbit.
2. In subtotal hepatectomy the rate of acetylation is reduced.
3. Following the intravenous injection of sulfanilamide in the bilaterally nephrectomized rabbit, a steady concentration of total sulfanilamide in the blood soon results, but acetylation progresses until the free form is present in only minimal concentrations.

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<sup>1</sup>Received for publication, August 31, 1938.

followed in many particulars the organization described by Fantus but have added several details which have improved the working of the blood bank in our hands. So much interest has been shown in the bank and so numerous have been the inquiries that we have been encouraged to report the details of the system as used at the Philadelphia General Hospital.

The advantages of the blood bank idea are many: (1) Citrated blood of any type may be obtained at any time in return for a similar quantity of blood. Thus, with a supply of blood on hand at all times, blood transfusion has become almost as simple as an intravenous infusion, differing only in the preliminary typing of the recipient and in the cross-agglutination test. (2) Typing and serologic determinations on the donor's blood are performed at the convenience of the laboratory workers and as part of their routine work. No unnecessary laboratory work is done, since every type of blood drawn will be used unless it is seropositive. (3) The confusion of having numerous donors in the hospital and the irregular interruptions of the intern's ward work are avoided by a systematic routine of collecting bloods.

#### SOURCE OF BLOOD FOR BLOOD BANK

The source of blood continues largely to be healthy relatives or friends of the patients likely to need blood transfusions. The relatives of such patients are requested by a clinical intern to have one or more donors come to the hospital at one of the donor clinics held three times each week. The intern is requested to inform the blood bank as to the number of donors expected to come to a clinic. From fifteen to twenty-five donors contribute blood at each of the three clinics. Interns on the dispensary service are assigned to duty in the clinic, which is under the supervision of the nursing personnel of the blood bank and the surgical resident.

Other sources of blood are the house or dispensary hypertensive patients with cardiac failure, on whom therapeutic venesections are performed; and, finally, placental blood has been obtained and used in relatively few instances. In spite of the fact that a relatively large number of transfusion bloods are needed, we have rarely found it necessary to obtain blood from the patients themselves as was recommended by Fantus.

#### DONOR CLINIC

Clinics for receiving blood are held three times weekly, from three to five o'clock on two afternoons and from seven to nine o'clock on one evening. The blood is drawn by the interns on dispensary service who are assigned to this duty by the chief resident physician for a period of two months. The clinic is in charge of the surgical resident, and the nursing staff is provided by the supervising nurse of the blood bank. With this arrangement a fairly uniform routine of taking and handling

bloods has been developed and the advantage of having a permanent nursing personnel familiar with the procedure is obvious. The donor clinic has been set up in a room adjoining the blood bank in order to facilitate the handling and depositing of the blood specimens.

Before the blood is drawn from the donor, a tag is filled out giving his name, age, and address, the date and the name of the patient for whom the blood is being given. At the end of the venesection, the amount of blood drawn is recorded. As soon as convenient, usually within ten minutes after completion of the venesection, the blood flask, properly capped and tagged and accompanied by its tube of citrated blood, is placed in the refrigeration vault.

The vault of the blood bank is an ordinary electric refrigerator housed in the solution room of the hospital. The temperature is maintained at 39° F. Each blood type has its own shelf, and flasks not yet in circulation, i.e., awaiting type and Kahn reports, are kept in a separate section. As soon as these reports are obtained, the results are noted on the flask card and the flask is then placed in circulation on its proper shelf. The bloods in the vault are inspected daily with a flash light for evidences of bacterial growth, hemolysis or clotting. Any specimen which is regarded as suspiciously unfit is discarded. At weekly intervals, bacterial cultures are made from flasks selected at random. Care is taken not to agitate the flasks unnecessarily as it has been apparent that repeated trauma increases the tendency toward hemolysis. An effort is made to keep the reserve supply in the bank at forty flasks. This has been found adequate for a hospital of 2,700 beds where an average of forty transfusions a week are done. In general, bloods of the same type are deposited and requested with like frequencies so that no effort has been made to control the type of donors.

#### BOOKKEEPING

For each flask of blood placed in the bank, a 3 by 5 inch card is filled out and placed in a Rand visual index file, the visible portion of each card bearing the donor's name, the amount in the flask, and the date the blood was drawn. Space is left on this portion for recording the type and serologic reports. The file is divided into five sections, one for each blood group and one for "Unreported Types and Kahns." When the type has been determined and the serology reported negative, these data are recorded on the card, which is moved to its proper section in the file. (When the Kahn test is positive the blood is, of course, discarded.) By means of such a file, bank assets are seen at a glance.

In addition to the Rand file, a large ledger is kept, with two pages assigned to each intern. A record of the deposits is entered in the left-hand column of each page; the withdrawals are recorded in red in the right-hand column. The ledger is balanced monthly and interns owing blood are requested to make up their indebtedness.

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ber of transfusions in this hospital, there seems to be no practical advantage in the direct method of transfusion of unmodified blood over the use of citrated blood.

*Apparatus for Drawing Blood.*—The method of removing blood from the donor was devised so as to make the system a closed one from the vein of the donor to the receiving flask. To this end, it was determined to remove the blood by suction from the vein into a tightly stoppered graduated Erlenmeyer flask. The essential piece of apparatus is a graduated liter flask with a three-hole rubber stopper fitted with glass tubing (Fig. 1). Each of two of the stopper holes accommodates a 4 cm. length of straight glass tubing. One of these is connected by a 15 cm. section of rubber tubing to a glass adapter which fits into the needle

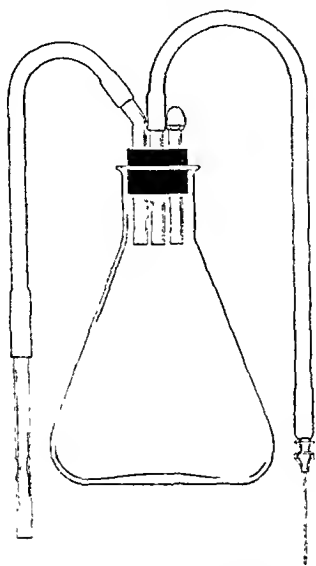


Fig. 1.—Donor apparatus.

in the donor's vein. The exposed end of the second straight glass tube is covered by a small rubber cap, such as an ordinary cystoscope tip. Through this rubber tip, anticoagulant may be injected into the flask without the loss of the partial vacuum. In the third hole of the rubber stopper is a 4 cm. length of glass tubing, the upper third of which is slightly bent. To this is attached a 15 cm. segment of rubber tubing in the end of which is a suction tip, consisting of a glass trap containing cotton or glass wool. In drawing blood, mouth suction is applied to the suction tip, thereby creating a small partial vacuum in the flask. Other equipment includes 3 towels, an 18-inch length of rubber tubing (tourniquet), Kelly hemostat, assorted needles (Nos. 21, 18, 16, 14, and hypodermic), one 2 c.c. syringe, one 20 c.c. syringe barrel fitted with a rubber (Asepto) bulb, 3 specimen tubes of 10 c.c. capacity, small cloth bag, printed tag, gauze squares, and roller bandage. This material, with

When a flask is sent from the bank to a patient needing blood, the corresponding card is removed from the file and held pending completion of the transfusion. After the desired amount of blood has been given, the patient's nurse fills out a questionnaire covering these essentials: (1) name of patient, (2) age, (3) indications for transfusion, (4) amount, (5) time required, (6) details of reaction, if any. The patient's temperature, pulse and respiration rates are charted half hourly on the same sheet. This form, together with the apparatus, is returned to the bank, where the data are recorded on the donor's card. This card is then filed in an "inactive" file. Thus, a record of every transfusion performed is available for any future reference.

#### OBTAINING BLOOD FROM THE BANK

When a transfusion is to be given, the type of the patient's blood is determined and the blood bank is advised that blood of that type is desired. The card file is consulted by the supervising nurse in the bank and the card of the proper type is chosen. The flask corresponding to this card is selected and the citrated sample of blood is removed from the small cloth bag attached to the flask. Two cubic centimeters of this sample are poured into a clean Wassermann tube and sent to the laboratory with a request for cross agglutination with the patient's blood which has previously been sent for typing. The remainder of the citrated sample of blood is replaced in the bag on the flask. If the cross agglutination shows the blood to be compatible with the recipient's, a notation to that effect is made on the donor's file card and the flask with the recipient's tray is sent to the patient's ward. If the cross agglutination shows that the blood is incompatible with the recipient's, the same routine is repeated, using another blood of the same type. After a cross agglutination a flask of blood may be reserved by an intern for a period of six hours. After that period it is considered that the transfusion is no longer necessary, and the blood is again placed in the general repository.

#### THE TECHNIQUE OF DRAWING AND GIVING BLOOD

The introduction of a blood repository or bank in which blood is collected, stored, and administered by several individuals has made it necessary to devise a method of carrying out this procedure which would offer the fewest technical difficulties and the greatest assurance of sterility. The apparatus here to be described and the method of handling and caring for the blood have been used with such success at the Philadelphia General Hospital since the establishment of a blood bank that it seemed worth while to publish the details of the apparatus and procedure.

Since the blood was to be stored, the citrate or indirect method of transfusion was chosen of necessity and in our experience in a large num-

ber of transfusions in this hospital, there seems to be no practical advantage in the direct method of transfusion of unmodified blood over the use of citrated blood.

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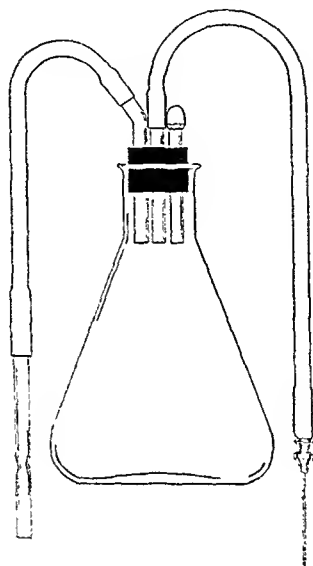


Fig. 1.—Donor apparatus.

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the flask and its stopper, constitutes the "donor's tray," which is autoclaved before use. Accessories not in the tray are sterile novocaine, 1 per cent, in a rubber-capped bottle, a 4-ounce bottle of sterile 2.5 per cent solution of sodium citrate, and a jar of gauze sponges immersed in 70 per cent alcohol.

*Drawing Blood.*—Venipuncture is executed by a doctor assisted by a nurse. The donor lies on a litter or table with the arm exposed on an arm board for six inches above the elbow. The doctor scrubs for three minutes and puts on sterile gloves. With the tray exposed, the nurse offers him the jar of alcohol sponges. Holding the sponges in the hemostat, the doctor cleanses the entire circumference of the donor's arm for a distance of six inches above and below the elbow. The arm is held elevated while a sterile towel is placed under it. On the towel is placed the rubber tube tourniquet; the arm is lowered. Sterile towels now cover the arm above and below the elbow. Using the 2 c.c. syringe and hypodermic needle, the doctor draws 1 c.c. of novocain from the rubber stoppered bottle held by the nurse and makes a wheal in the skin at the site of the proposed venipuncture. The patapar\* cap is now removed from the liter flask and 20 c.c. of the sodium citrate solution are added to the flask with the 20 c.c. syringe. The syringe is now handed to the nurse who subsequently adds additional citrate as needed. With the stopper in the flask, the tourniquet is tightened, a needle of large bore, usually a No. 14, is fitted to the glass adapter and the needle inserted into the vein. Suction on the mouthpiece at this point will create a partial vacuum in the flask, and as the blood flows the flask is constantly agitated in a swirling motion. When 200 c.c. have been drawn, and if the flow appears free, a second 20 c.c. portion of sodium citrate is added. This is done by the nurse, who inserts the needle of the large syringe through the rubber tipped tube and injects the contents into the flask. She immediately refills the syringe as before. When 400 c.c. of blood are in the flask, she injects 10 c.c. more of anti-coagulant. Thus a total of 50 c.c. of 2.5 per cent solution of sodium citrate has been put in the flask, enough to prevent the clotting of 500 c.c. of blood. (Interns are requested to remove not more than 500 c.c. from one donor.) While she is awaiting the completion of the procedure, the nurse removes the three specimen tubes from the tray, removes the plugs, and injects 0.5 c.c. of sodium citrate solution into one of them.

When the full complement of blood has been drawn, the glass adapter is removed from the needle and the flask set aside. The three specimen tubes are given to the doctor, who half fills each with blood flowing from the needle still in the donor's vein. The needle is now removed and a sterile dressing applied to the arm. The doctor removes the stopper

\*Patapar is a vegetable parchment paper. The cap is fastened over the mouth of the flask with an elastic band before autoclaving.

from the flask and replaces the sterile patapar cap, fastening it with a rubber band. The small cloth bag is slipped over the flask and the specimen tube of citrated blood, labeled with the donor's name, is placed in it. This tube remains with the flask and is to be used for cross agglutination. The tag is filled out and tied on the flask. The remaining clotted specimens are sent to the laboratory, one with a request for typing, the other for a serologic test. The flask of blood is taken at once to the solution room where a reinforcing gauze dressing is placed over the mouth; it is placed immediately in the refrigerator.

This method of collecting blood limits as much as possible any chance contamination of the blood. Citrate may be added as needed without interfering with the partial vacuum and in this way an excess of anticoagulant may be avoided. Blood is collected separately for typing and for serologic examination, and a third marked tube containing citrated blood is attached to the flask which may be used for cross agglutination without the necessity of disturbing the stored flask.

*Blood Transfusion.*—For the administration of the blood an effort was made to devise a system which would permit the use of physiologic saline solution preliminary to the administration of the blood to insure an air-free system and to facilitate venipuncture. In addition, provision was sought for the following features: (1) The blood container should remain upright at all times to avoid spilling. (2) An easily readable method for judging and regulating the speed of administration should be provided. (3) Opportunity should be given for the administration of saline or glucose solution in any desired amount through the same apparatus without disturbing it.

To meet these requirements a system was devised modeled much after that described by Milroy and Matheson, of Australia,<sup>2</sup> in which saline solution could be given through a small trap or reservoir, to be followed by blood drawn from the flask by siphonage. The siphon withdrawal allows the blood flask to remain upright and its drop into the small reservoir permits an accurate estimation of the speed of the transfusion. A Hoffman clamp on the siphon tube is used for easy regulation of the rate of flow. Additional infusion fluid to follow the blood is poured into the original blood flask through a small glass funnel which also acts as an air vent.

In attempting to make the apparatus as cheaply as possible, the barrel of the "Triumph" type of irrigating syringe was found to be suitable for use as a small reservoir. The cone shape of the Erlenmeyer flask makes it convenient to fit on it a holder for the reservoir by using a metal ring which will rest well down on the flask.

When proper cross-agglutination results have been obtained between the patient's blood and the donor's blood removed from the citrated tube

on the flask, the flask of blood and a recipient's tray are sent to the patient's ward. The autoclaved tray which accompanies the flask of blood to the patient contains a two-hole stopper with glass tubing; a glass reservoir (syringe), with attached 30-inch length of rubber tubing and needle adapter; a metal ring to fit over flask; three towels; rubber tube tourniquet; Kelly hemostat; assorted needles (Nos. 21, 18); gauze squares and roller bandage. Accompanying the tray is a jar of gauze sponges in 70 per cent alcohol. Through the two-hole rubber stopper pass a short stemmed glass funnel and a thistle tube which reaches just to the bottom of the flask when the stopper is in place. Four thicknesses of fine mesh gauze are tied over the end of the thistle. This filter is

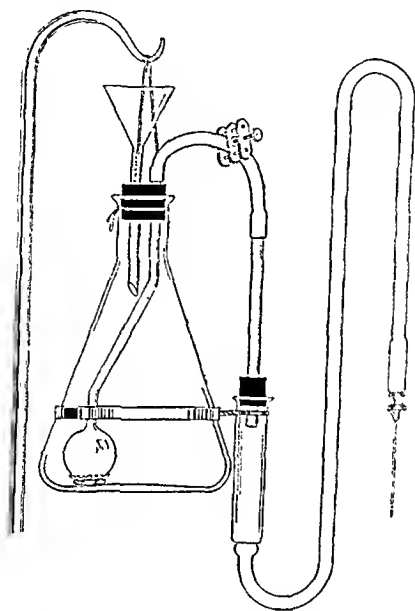


Fig. 2.—Recipient apparatus.

renewed after each transfusion. The outer end of the thistle tube connects with a 12 cm. length of straight glass tubing by means of a 15 cm. segment of rubber tubing. A Hoffman clamp is included in this section of rubber. The open end of the straight glass tube passes just through a rubber stopper which fits snugly into the Triumph syringe barrel (reservoir). (Fig. 2.)

After antisepsis of the recipient's arm in the same manner as that described for the donor's arm, and after warming the blood to near body temperature by placing the flask in water at 105° F., the metal ring is placed over the flask. (This ring is actually a double ring of metal constructed in the form of the figure 8 with one small aperture and one large one.) The covering of the flask is removed.

After the two-hole stopper is firmly inserted, the flask is suspended about three feet above the bed by means of two tapes fastened around the neck. The long section of rubber tubing attached to the reservoir is passed through the small aperture of the ring, bringing the lip of the reservoir to rest on the ring. A needle is fixed to the glass adapter at the distal end of the tubing. Warm physiologic saline solution is now poured into the reservoir, nearly filling it. After the tubing and needle have been made airfree, the recipient's vein is entered while the nurse pinches the delivery tube. When the needle is in the vein, as shown by a backflow of blood in the adapter, the tourniquet is removed and pressure on the delivery tube is released. As the level of saline solution in the reservoir falls, the rubber stopper is fitted in the reservoir. The falling head of saline solution draws blood over into the reservoir through the thistle tube, creating a siphon. As the blood passes through the gauze covering the thistle, it is filtered. The rate of flow may be adjusted by the Hoffman clamp. The siphon drip in the reservoir can be observed as readily as the flow in a Murphy drip bulb, making it easy to gauge the rate of flow. No blood is left in the flask if the thistle grazes the bottom of the flask. If it is desired to follow the transfusion with an infusion, the solution may be added to the flask through the funnel.

The advantages of this method of transfusion are several. The system is open to a minimum of contamination from without. The use of the preliminary saline solution makes it possible to clear the system of air with certainty. In addition, the transfuser may be sure that his needle is in the vein and that the flow is free before the blood flow is started. The possibility of adding other solutions without disturbing the apparatus makes it convenient to give as much fluid as desired without disturbing the needle in the vein or the apparatus. There is no pouring or dripping or spilling of blood.

*Placental Blood.*—Our technique of collecting fresh placental blood for use in transfusions is much the same as that recently described by Goodall and his co-workers of Montreal.<sup>3</sup> After the delivery of the baby, the cord is divided between two clamps in the usual manner. The maternal portion of the cord is then cleansed with 70 per cent alcohol for a distance of 8 inches proximal to the clamp. A sterile drape, measuring 40 by 18 inches, having a small hole in its center, is then placed across the perineum, and the clamped end of the cord passed through the hole for a distance of 6 inches. The cord is now cut proximal to the clamp and the blood collected in a 250 c.c. Erlenmeyer flask, to which has previously been added 8 c.c. of 2.5 per cent sodium citrate solution. The flask is agitated to insure proper citration of the blood. The flask is capped, labeled, and taken at once to the refrigerator of the blood bank. Administration of this blood as a transfusion is effected through the usual recipient's tray.

## SUMMARY

A technique of blood transfusion is described for use in connection with a blood bank. It has the following features:

1. A nearly closed system offering minimal chances of contamination.
2. Blood is drawn into, stored in, and delivered from a single flask.
3. The drawing of blood is facilitated by means of suction.
4. Sodium citrate is added to the flask as the blood enters, thus avoiding too high a concentration of anticoagulant.
5. Administration of the blood is preceded by a small saline infusion, whereby the tubing is cleared of air and which permits accurate placing of the needle in the recipient's vein before the blood is allowed to run.
6. The apparatus used is described in detail.
7. A technique for collecting placental blood is described.

## RESULTS IN 1,000 TRANSFUSIONS USING CITRATED REFRIGERATED BLOOD

The data here presented are based upon our experience in the first 1,000 transfusions given through the agency of the blood bank. In order to provide 1,000 usable specimens of blood, blood was drawn from 1,123 donors. Amounts of blood varying from 250 to 600 c.c. were obtained, the average quantity being about 450 c.c. The incidence of each blood group is shown in Table I.

TABLE I  
INCIDENCE OF BLOOD GROUPS IN 1,123 DONORS

Type I*	3.3%
Type II	32.2%
Type III	15.0%
Type IV	49.5%

\*Moss classification

One hundred and twenty-three specimens of blood (11 per cent) were not used for transfusions. The reasons for this loss are given in Table II. Those marked unsuitable laboratory specimens are those in which an insufficient quantity of blood was drawn, where the specimen hemo-

TABLE II  
SOURCES OF LOSS IN BANKING 1,123 BLOODS

	NUMBER	PER CENT
Seropositive	53	43
Unsuitable laboratory specimens	20	16
Aged	25	20
Hemolyzed	17	14
Cultured	6	5
Broken	2	2
Total	123	100

lyzed rapidly or where a specimen which was sent for serologic testing had been citrated by mistake. It was interesting to note that only 25 of the 1,123 deposits (2.2 per cent) were discarded because of age. Speci-

mens were discarded when they had remained in the refrigerator for 5 weeks. The average flask of blood remained in the refrigerator for 5 days before its use for transfusion. Naturally the preservation time was shortest in the commoner blood groups; the flasks in Groups II and IV were usually called for and used for transfusion within 24 to 48 hours after they were placed in the refrigerator. On the other hand, the bloods discarded because of age were almost exclusively of Group III.

Regarding hemolysis, it appears that this tendency is unpredictable and is entirely an individual variable. Some specimens showed beginning hemolysis as early as 2 days after withdrawal. Many others showed no evidence of hemolysis at the end of 7 weeks of refrigeration.

Cultures made from blood specimens taken at random from the refrigerator have been consistently negative. In addition, cultures made from blood remaining in a flask following transfusion reactions likewise have been negative with two exceptions. One of these showed a growth of *Staphylococcus aureus*. The other resulted in a growth identified as *Streptococcus viridans* and a diphtheroid bacillus. In both of these cases in which positive cultures were obtained, the flasks were open to contamination before the cultures were made, having stood open and unprotected throughout the night and having been freely manipulated by unsterile hands.

The incidence of reaction has been relatively low (7.4 per cent). We have classified the reactions as mild, severe, and allergic. A mild reaction is one which is accompanied by a temperature not exceeding 101° F., at times associated with a feeling of chilliness and vague unrest. A severe reaction is manifested by a temperature elevation of over 101° F., a frank chill, a decrease in pulse volume, and an increase in pulse rate. An allergic reaction presents chiefly urticarial phenomena, occasionally with a slight temperature elevation, and rarely with a chill. The frequency of these untoward results of transfusion is tabulated in Table III. We have not noted any increase in the frequency of reactions in blood which has been refrigerated for longer periods of time (2 to 3 weeks).

TABLE III  
REACTIONS IN 1,000 TRANSFUSIONS USING CITRATED REFRIGERATED BLOOD

	NUMBER	PER CENT
Mild	29	2.9
Severe	28	2.8
Allergic	17	1.7
Total	74	7.4

#### SUMMARY

We have described in detail the routine of the working of the blood bank of the Philadelphia General Hospital. The advantages of the bank idea are many. The source of the blood is usually healthy relatives of patients. Blood is drawn at regular donor clinics and im-

mediately deposited in a refrigerator. The bookkeeping of the bank has been described.

The technique of an almost closed system for the use of the citrate method in the blood bank has been described.

The results in 1,000 transfusions given by the method described have been analyzed. In giving 1,000 transfusions, blood from 1,123 donors was drawn. Eleven per cent of these were not used for transfusion.

Reactions occurred in 7.4 per cent of the 1,000 transfusions.

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## OPERATION FOR DISLOCATED SEMILUNAR BONE OF THE WRIST

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**D**ISLOCATION of the semilunar bone, while not extremely rare, is an injury more frequently overlooked than correctly diagnosed. The purpose of calling attention to this lesion again is threefold: the fact that the interpretation of findings by the surgeon or roentgenologist is frequently incorrect, leading to a deficient diagnosis; to emphasize the clinical and roentgenologic diagnostic features, each of which is typical; and third, to show that the proper method of treatment, if reduction by manipulation fails, is open operation with replacement of the bone in its normal location, not excision of the semilunar bone. One of us (H. R. M.) has seen 5 cases since 1933 which have been diagnosed mistakenly by one or more doctors before the lesion was recognized. In the records of patients admitted as in-patients to Charity Hospital since 1926, there are 15 cases with a diagnosis of dislocation of the semilunar bone. Cases reduced in the emergency service and sent to the clinic as out-patients are not included in this.

In the Tulane Fracture Clinic of Charity Hospital, which includes only part of the white male fracture service, there have been 649 cases treated during the last two years. Among this group there were 2 cases of dislocation of the semilunar bone; an incidence of 1 in 325 cases; 3 cases of fractured scaphoid of the carpus, 2 of which were associated with the above dislocations.

Of the 15 cases with dislocated semilunar bones admitted to the hospital since 1926, 13 were males; 2 were females. In 9, fracture of the carpal scaphoid was associated with dislocated semilunar. Of 5 cases operated upon by one of us (H. R. M.) and reported herein, 4 (80 per cent) had an associated fracture of the scaphoid. A fracture of the carpal scaphoid is more often correctly diagnosed than a dislocated semilunar bone by the inexperienced surgeon, and, if both lesions coexist, the dislocated semilunar may be overlooked even though the fractured scaphoid is recognized. Once we encountered a case subsequent to the removal of the proximal fragment of a fractured scaphoid as a procedure of election by another surgeon, who had overlooked the dislocated semilunar with which the fractured scaphoid was associated.



The type of injury causing dislocation of the semilunar bone was recorded in 12 of the 15 cases as follows: direct blows on the back of the hand, 5; falls, presumably on the outstretched hand, 4; automobile accidents in which the exact mechanism was not explainable by the patient, 3; no history of the type of injury was recorded in 3 instances. The importance of the type of injury producing this lesion has been grossly overemphasized. Presumably from the displacement of the bone anteriorly it has been reckoned that the injury is the result of hyperextension of the hand, the head of the capitate squeezing the lunate forward and breaking the posterior radiolunate ligament. This, however, is presumptive and, as in many other fractures, certain authors apparently get assistance in revealing to themselves the type of trauma from the lesion, rather than assistance in diagnosing the lesion from the type of trauma. In the production of dislocation of the semilunar bone, the injury apparently can be of several varieties; thus, in the 15 cases hyperextension is recorded with reasonable certainty only in 4 instances; whereas, direct injury on the dorsum of the wrist is recorded in 5. If one is careful in questioning the patient about the direct mechanism of injury, it will be proved conclusively that not 10 per cent of the patients can give the story of the details of an accident with even the slightest degree of certainty. These lesions can as well be diagnosed accurately with the story that the patient has hurt his wrist, as when the mechanism is indicated by the patient as being a fall on the outstretched hand or a blow on the back of the wrist.

*Characteristic clinical features of dislocations of the semilunar bone* are as follows: The wrist appears thickened anteroposteriorly. There is a prominence on the volar surface. The increase in anteroposterior diameter is greater than can be attributed to the soft tissue swelling. Moreover, the prominence of the wrist is resistant, not compressible. The fingers are held paralytically in slight flexion, and, because of pain, there is very little motion in the hand and wrist. (Figs. 2 and 5.) Attempts at motion result in so much pain that 15 degrees of flexion or extension of the fingers or wrist may be the limit, particularly in recent injuries. Radial and ulnar deviations of the hand are likewise limited. There may or may not be subjective numbness and obtunded sensation over the index and middle fingers and the radial side of the fourth finger due to pressure on the median nerve. Even in old cases the patient complains of weakness of the hand and wrist and the grip is extremely weak. Over the carpus anteriorly is found a resistant prominence and posteriorly just distal to the radius an abnormal fossa might be palpable, though it may not be visible due to swelling. Pressure in the anatomic snuffbox may reveal exquisite tenderness which suggests that, together with the dislocation of the semilunar bone, there is a fracture of the carpal scaphoid. The three main features of the objective findings in dislocated semilunar are: (1) the increased promi-

nence of the wrist anteriorly; (2) characteristic position of the hand, with the wrist held straight and the fingers slightly flexed and relative immobility in this position; and (3) the palpable prominence of the semilunar bone anteriorly under the anterior carpal ligaments. The characteristic appearance of thickened straight wrist and slightly flexed painfully fixed fingers is almost diagnostic. None of these findings, however, will leave full assurance of the correct diagnosis without the x-ray.

Roentgenograms reveal the true diagnosis in a suspected dislocation of the semilunar bone. The anteroposterior view may show overlapping of the semilunar and the head of the os magnum, or the semilunar may be displaced more extensively as is shown in Fig. 3. The lateral view of the normal wrist shows very distinctly the head of the os magnum fitting into the concavity of the semilunar with the semilunar convexity articulating with the radial articular surface. This lateral roentgenographic view reveals the conformity from which the bone received its name. In dislocation of the semilunar, lateral roentgenograms show the bone displaced anteriorly with a concave surface usually pointing forward and the convexity jutting against the head of the os magnum. The bone is generally so close to its normal position, however, that the inexperienced eye may overlook a perfectly obvious dislocation. To one who has not seen the lesion previously it can be discerned only by being aware of the possibility of its presence and looking for the normal relations. Occasionally the semilunar will be displaced widely. In such instance it may be found above the lower margin of the radius and above the anterior annular ligament of the carpus (Fig. 3). Dislocation of the semilunar bone itself is more common than posterior dislocation of the head of the os magnum, in which instance the semilunar retains its normal relationship to the radius. The proximal fragment of a fractured scaphoid is frequently dislocated forward with the lunate. This occurred in two of our five cases. Such a dislocation is simultaneously and spontaneously replaced when the lunate is reduced even though the reduction be by open operation. Other fractures, notably that of the radial styloid may occur with dislocated semilunar. This happened twice in our five operated cases. In one case the base of the fourth metacarpal was fractured. Whenever a dislocation of the semilunar is found, the scaphoid bone should be carefully inspected in the roentgenogram to determine if a fracture of this bone is coexistent, because, as demonstrated by the figures presented, an associated fracture may be found in from 50 to 80 per cent of the cases. Oblique views may show some fractures of the scaphoid more clearly. Fracture of the scaphoid necessitates more prolonged immobilization after reduction than if the semilunar dislocation is uncomplicated.

## TREATMENT

Several methods have been advocated for reducing dislocations of the lunate bone. All reductions of course are attempted under anesthesia. The methods deserving mention are: (1) Hyperextension of the hand, with pressure by the operator's thumb on the lunate distally and backward to re-engage the posterior lip of the semilunar under the head of the os magnum. When this is accomplished, the hand is flexed and then put into a position of optimum function for immobilization. The Thomas wrench has been recommended for hyperextension. A modification of this method is the use of a broom handle, rolling it distally across the volar surface of the wrist while the hyperextended hand is slowly flexed, at the same time exerting traction distally on the fingers. This procedure is not recommended because it is likely to traumatize the structures severely without accomplishing reduction. Proof of complete reduction must be obtained by the roentgenogram. (2) In a second method the operator hyperextends the hand and presses distally on the dorsum of the patient's hand at the head of the os magnum to increase the distance between the radius and os magnum. The semilunar bone is pressed backward and distally by the operator's other thumb. After the head of the os magnum slips over the posterior lip of the semilunar bone and into its concavity, the hand is flexed and immobilized in a neutral position. (3) Böhler<sup>1</sup> recommends traction in the longitudinal axis of the arm, on the thumb and fingers, with the patient under deep anesthesia, continuing the traction for a period of at least ten minutes. When the space between the capitate and radius is increased sufficiently, the flexor tendons press the semilunar back into position. (4) Open reduction; and (5) excision.

In very recent cases reduction by manipulation under anesthesia is almost always obtainable. However, after a period of a few days or weeks, when the reaction to trauma has begun to firmly establish new conditions, reduction by manipulation, even under deep anesthesia, may be difficult or impossible. Numerous rough attempts at closed reduction should not be persisted in as the open operation can accomplish reduction with certainty and with less trauma. Unfortunately many authors and many more operators consider an *unreduced* semilunar bone a prize to be removed, stating that function after removal of the semilunar will be almost as good as if the semilunar were in place. Function is never as good as if the semilunar is accurately replaced, and replacement can be accomplished by an open operation. In almost all instances the posterior ligament between the radius and lip of the semilunar bone is torn, but the anterior ligament remains intact. As has been shown by Conwell,<sup>2</sup> as well as by our series, replacement of the bone results in no subsequent atrophy or disturbance

of calcification. Even if the semilunar bone is found at operation to be entirely unattached to any tissue, until it is proved otherwise, replacement seems better than removal.

#### THE OPERATION

Beginning proximal to the proximal transverse furrow on the anterior surface of the wrist and between the tendon of the palmaris longus and flexor carpi radialis, an incision is made which runs distally for a distance of approximately 4 cm. onto the hand just to the ulnar side of the tuberosity of the scaphoid (Fig. 4). The anterior annular ligament is incised and the flexor sublimis and flexor profundus tendons are displaced together with the median nerve to the ulnar side. The dislocated semilunar bone will be found as a prominence and the concave glistening articular surface will be easily recognized. After incising the fibrous tissue over the carpal bones between the scaphoid and os magnum, the head of the os magnum becomes clearly visible as the semilunar is rotated forward. A curved periosteal elevator is inserted under the head of the os magnum while hyperextending the hand. Pressure on the posterior lip of the semilunar with a blunt pointed elevator while the head of the os magnum is being elevated will allow the bone to recover its normal position, with relation to the radius and os magnum. After the periosteal elevator is removed, the head of the os magnum engages in the concavity of the semilunar. This relatively simple procedure completes the operation except to close the anterior annular ligament, the subcutaneous tissue and skin, with interrupted silk sutures. The wound is dressed with xeroform gauze (gauze impregnated with 5 per cent xeroform powder in white vaseline), and the hand is immobilized with a skin cast extending from metacarpophalangeal joints to the upper third of the arm. Immobilization is continued for approximately three weeks if a dislocation alone exists; for eight weeks if there is an associated fracture of the scaphoid.

The abstracts of the case histories of the five cases operated upon by one of us are as follows:

CASE 1.—F. V., white male, aged 42 years, was admitted to Charity Hospital on June 13, 1933. On June 10, while repairing an automobile, an engine block slipped off a jack and fell on his hand. His hand pained him severely; more toward the radial side of the wrist. He was seen in the accident room where a diagnosis of Colles' fracture was made. He was not admitted to the hospital until three days later. X-ray showed fracture of proximal and fourth metacarpals and the styloid process of the ulnar and anterior dislocation of the left semilunar carpal bone. The left wrist was markedly swollen. There was a small laceration between the fourth and fifth knuckles on the dorsum of the hand, and marked impairment of motion of the wrist. No evidence of deformity was described. An attempt at closed reduction made on June 15 failed. Open reduction was done on June 17, seven days after the accident. The operation described above was performed, with replacement of the semilunar bone (Fig. 1). However, catgut was used instead of silk which we

now employ. Subsequently the man had an uneventful convalescence and recovered perfectly. He is now driving a moving van with no impairment of motion whatsoever in his wrist and no weakness or pain.

CASE 2.—H. L., aged 27 years, a white male, was admitted to the hospital on Jan. 3, 1935. On Nov. 26, 1934, he was struck on the back of the left hand with a chair. He had pain for two weeks constantly and after then at intervals and at night. He had been unable to use his hand and any wrist motion caused pain. Diagnosis

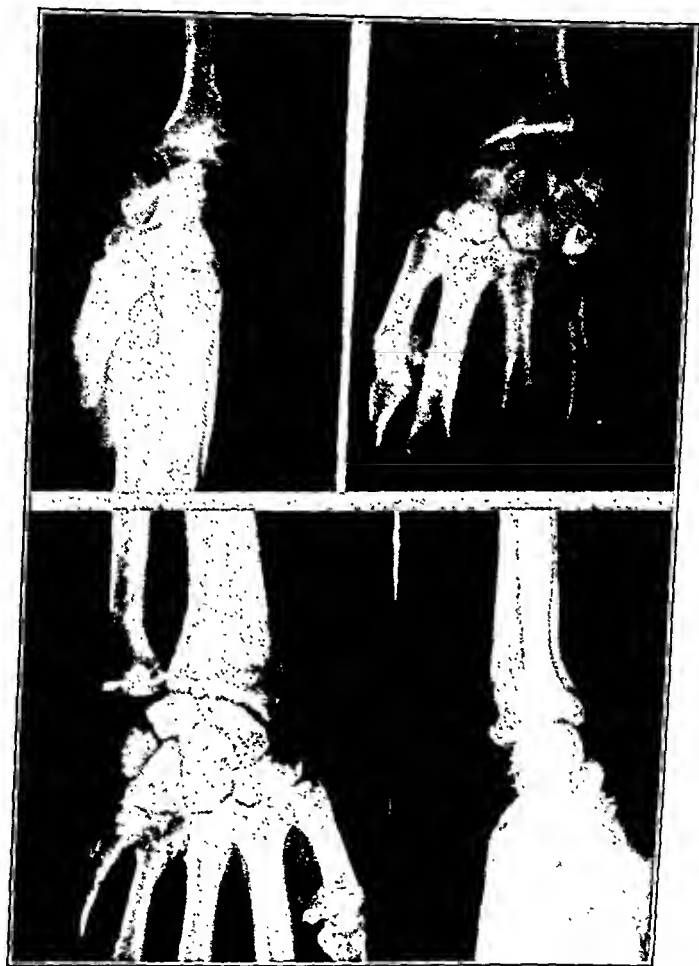


Fig. 1.—Dislocation of the carpal semilunar bone with associated fractures of the fourth metacarpal and styloid process of the ulnar (Case 1). Above, showing the semilunar dislocated with the concavity turned sharply forward; below, after operative replacement. The head of the os magnum fits into the concavity of the semilunar. Note that the fracture of the fourth metacarpal is united.

had not been made before the patient's admission to the hospital. Examination showed swelling and prominence anteriorly on the wrist. The hand was held in extension, the fingers slightly flexed; voluntary motions of the fingers and the hand were extremely slight. Roentgenograms of the left wrist showed a dislocation of the semilunar bone and a fracture of the scaphoid. No attempt at closed reduction was made because of the lapse of time since the injury. The operation described above

was performed six weeks after the initial injury, and the semilunar bone was replaced. A skin cast was applied and immobilization was continued for eight weeks. Subsequent x-rays showed the bone to be in good position with union of the fractures of the scaphoid and the styloid of the ulnar (Fig. 2). This patient had complete recovery of function without any residual disability whatsoever.

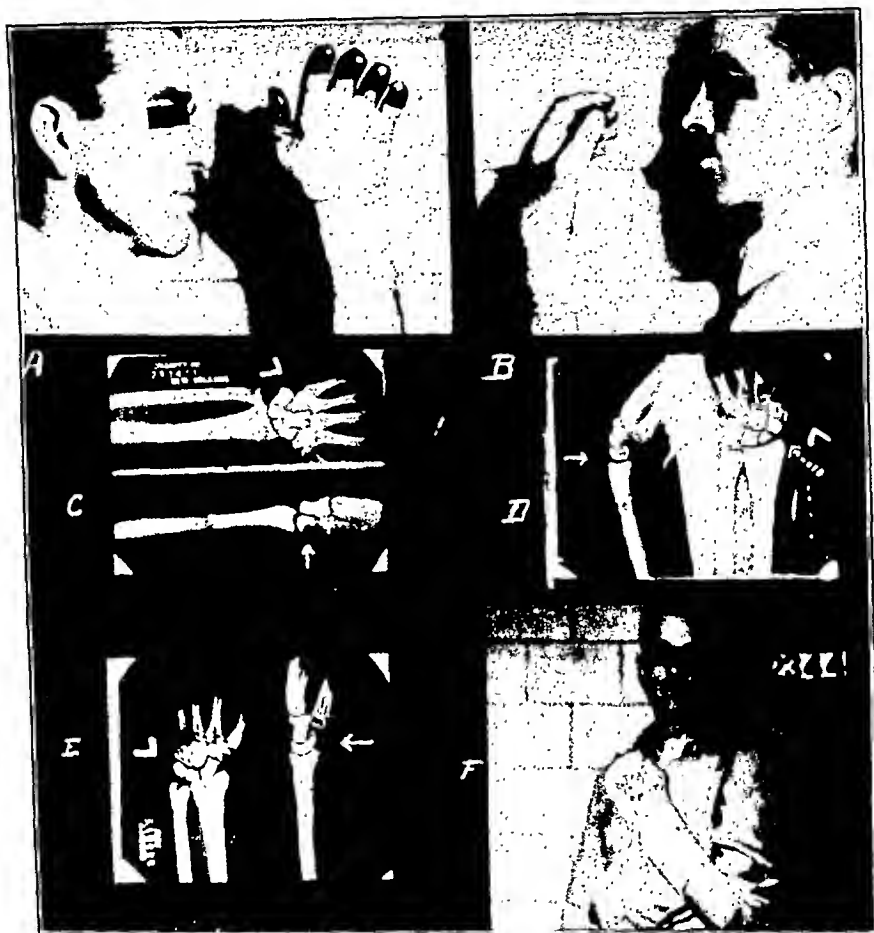


Fig. 2.—(Case 2.) A and B, Appearance of the hand before reduction of dislocation of the carpal semilunar bone. The wrist is thickened at the carpus and the fingers are held in slight flexion with a relatively straight wrist. Because of pain there is very little motion of the fingers or wrist. C, Retouched x-ray showing the concavity of the semilunar bone turned forward and the head of the os magnum posterior to its normal position. There is a fracture of the scaphoid. D, After operation, showing the head of the os magnum fitting into the concavity of the semilunar. Because of ulnar deviation of the hand, the fragments of the carpal scaphoid are widely separated. E, Radial deviation of the hand has approximated fragments of the scaphoid which are now united. F, Patient shown in type of cast used for immobilization, which should be continued for eight weeks if there is an associated fracture of the carpal scaphoid.

CASE 3.—L. A., aged 33 years, white male, was admitted to Charity Hospital Oct. 8, 1936. Eighteen months previously he had fallen from a scaffold and hurt his wrist. He had continued to have pain in the wrist and weakness of his hand, but, though numerous doctors had seen him, the correct diagnosis had not been made. Examination at the time of admission to Charity Hospital showed limitation

of motion of the wrist in all directions and weakness of the grip. There was a prominence anteriorly on the carpus, which, on pressure, caused marked pain which radiated distally into the index and middle fingers. Roentgenograms showed dislocation of the semilunar bone and fracture of the scaphoid. Though the bone had been out of position for eighteen months, replacement was attempted at open operation. It was possible to engage the head of the os magnum in the concavity of the semilunar, but it was impossible to hold it in this position without flexing the wrist. Flexion of the wrist was maintained for a period of eight days during which time x-rays showed the head of the os magnum to be in the concavity of the semilunar. Extension of the hand, however, after eight days resulted in redislocation of the semilunar bone. The semilunar was subsequently removed. There was slight improvement following this, particularly in the disappearance of the shooting pain which the patient previously had on pressure over the carpus and in the numbness which had persisted prior to excision of the bone. Function, however, was never



Fig. 3.—An unusual case of dislocation of the carpal semilunar bone (case of Dr. H. Theodore Simon). Such wide displacements are uncommon but occasionally do occur. The procedure of choice is not excision of the semilunar bone, but replacement either by manipulation or by open reduction.

good. The patient worked as a longshoreman prior to injury, but has not been able to do hard work with the hand since. He still complains of weakness of his hand and tenderness over the carpus. Motions are limited in all directions.

CASE 4.—C. U., aged 19 years, a white male, admitted to the Charity Hospital May 17, 1937. On May 16, 1937, he was hurt in an automobile accident, and had pain in both arms. He had been treated elsewhere for lacerations and bruises and his right arm was in a splint. Removal of the splint showed swelling of the fingers and the hand, tenderness at the lower end of the radius with marked limitation of motion in the wrist. X-ray showed fracture of the scaphoid with displacement and overlapping of the fragments and anterior dislocation of the semilunar bone. Open operation was done after attempts at closed reduction failed. The semilunar bone was replaced as described above and likewise simultaneously the fragments of the fractured scaphoid came into accurate position. Subsequent x-rays showed union of the navicular fracture and the lunate bone to be in good position without evidence of atrophy. The patient made an uneventful recovery and had no residual disability whatsoever.

CASE 5.—B. H., aged 57 years, a white male, was admitted on Feb. 16, 1938. On Jan. 8 he had been hit on the back of the hand by a crank while he was cranking a car. The handle swung around and hit him on the back of the hand. Pain was not severe. The next day he went to the hospital. He had a splint applied. The emergency officer, apparently not sensing the type of injury, did not have an x-ray taken. He was told to return in three weeks. He returned after that time to the

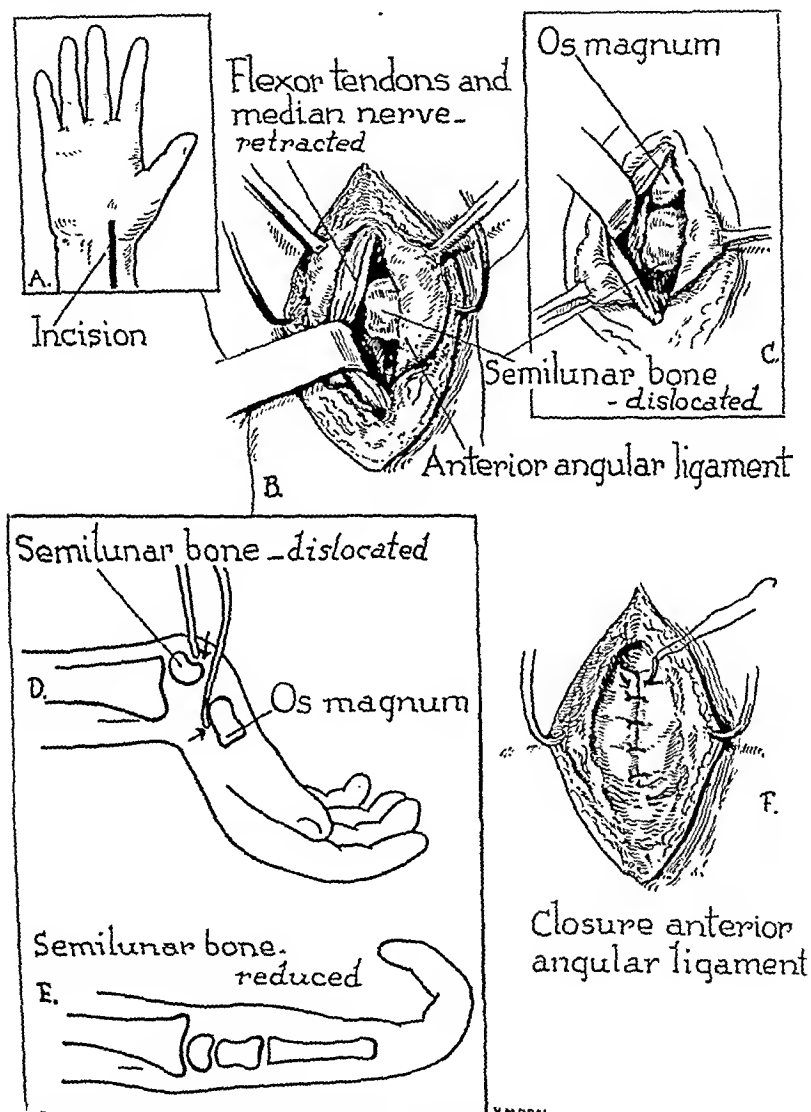


FIG. 4.—Operation for replacement of a dislocated semilunar bone irreducible by manipulation. A, The line of incision is just to the ulnar side of the tendon of the flexor carpi radialis. B, After incising the anterior angular ligament, the flexor sublimis and profundus tendons with the undiscovered median nerve are retracted to the ulnar side. This exposes the glistening concavity of the dislocated semilunar. C, The capsular fibers overlying the os magnum are incised, exposing the smooth head of the os magnum. D, With the hand hyperextended and with the aid of a curved elevator the head of the os magnum is elevated while pressure is made posteriorly on the distal (posterior) lip of the dislocated semilunar. E, The position when the bone has been reduced. F, The annular ligament and wound are closed with interrupted silk sutures.



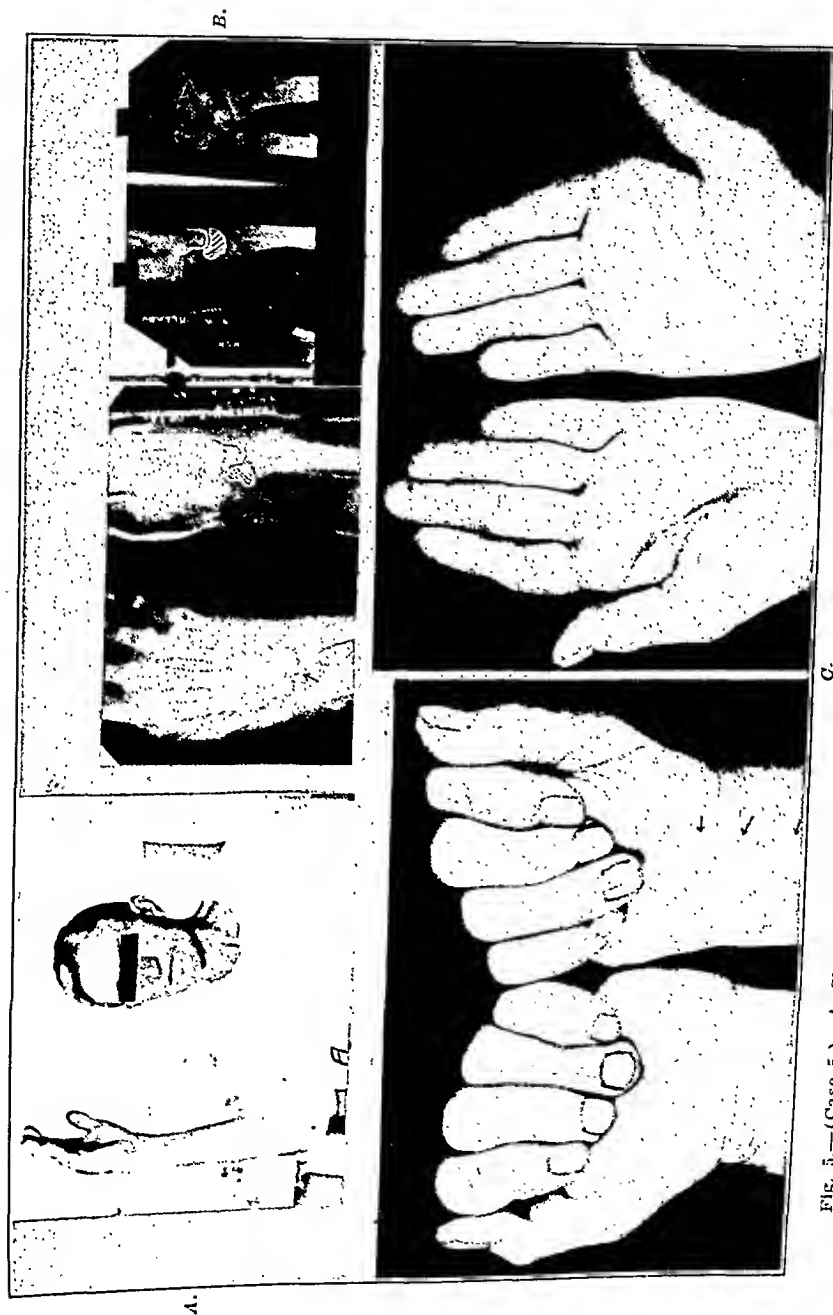


Fig. 5.—(Case 5.) A, Shows the patient with characteristic appearance of the hand with dislocation of the carpal semilunar bone. The wrist and the fingers are held in slight flexion with very little motion as is also shown in Fig. 2. Such an appearance is characteristic of dislocated carpal semilunar bone. B, The x-rays before and after operation and replacement of the dislocated semilunar. The semilunar bone is shaded. In the preoperative view the convex head of the os magnum is seen behind the displaced semilunar; whereas in the postoperative view, the head of the os magnum fits in the concavity of the semilunar. Note that the displaced fragments of the fractured scaphoid is in good position in the postoperative x-rays. X-rays have been slightly retouched to insure clarity. C, The patient's hands after full recovery. There is no residual disability. Note the scar of the incision indicated by arrows.

clinic. Objective findings showed swelling, especially of the wrist, with a prominence anteriorly. The hand was held in extension with pitifully little motion of the wrist and fingers. Motion caused pain. He could flex fingers to 30 degrees only. The thumb could scarcely be moved at all. On the anterior surface proximal to the thenar eminence was a hard immovable mass about the size of an almond. X-rays showed dislocation of the semilunar bone anteriorly and a fracture of the scaphoid. An open reduction was done as described five weeks after the accident. The bone was replaced and immobilization was continued for eight weeks (Fig. 5). Union of the scaphoid followed promptly. He had an uneventful convalescence and complete range of motion and full function returned.

#### SUMMARY

It is thus shown that of 5 cases in which the semilunar bone was replaced by open operation, 4 in which the operation was done within a reasonable time (longest, six weeks after the injury) had perfect results. The fifth case, in which the dislocation had existed for eighteen months, had a poor result and the semilunar bone had to be removed. If reduction of the dislocation of a semilunar bone of the wrist cannot be accomplished by manipulation, open operation is indicated with replacement of the bone in its normal position, not removal of the bone.

The clinical and roentgenologic features of the lesion are described.

An operation for replacement of the dislocated semilunar is described.

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# THE EFFECT OF EXPERIMENTAL HYPERTHYROIDISM AND HYPOTHYROIDISM UPON THE CONCENTRATION OF CHOLESTEROL IN HEPATIC BILE\*

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CONSIDERABLE evidence has been presented in the literature to show that the formation of gallstones is preceded or accompanied by hypercholesterolemia. For example, Boyd<sup>1</sup> has reported hypercholesterolemia during the latter months of pregnancy, a condition in which the first symptoms of gall-bladder disease are very frequently manifested. Moreover, data from this laboratory<sup>2</sup> indicate that the cholesterol concentration in the gall-bladder bile of pregnant women at term is above normal. Among others, Fowweather and Collinson<sup>3</sup> and Bockus, Willard, and Metzger<sup>4</sup> report that gallstone disease is frequently accompanied by a hypercholesterolemia.

These studies carry with them the implication that a high blood cholesterol level affects the concentration of cholesterol in the bile, either by increasing the cholesterol in the hepatic bile or by adding cholesterol to the bile in the gall bladder.

Opposed to this theory are the findings of other workers. Andrews,<sup>5</sup> Campbell,<sup>6</sup> and Ravdin,<sup>7</sup> for example, have found that gallstone disease is not commonly accompanied by hypercholesterolemia. This, of course, does not rule out the possibility that a high blood cholesterol might have existed at the time stones were first formed. Gardner<sup>8</sup> reported that autopsies on a group of patients dying from lipoid nephrosis, a condition in which the blood cholesterol is very high, showed that gallstones had not occurred in these cases.

It seemed that, before any conclusion could be drawn as to the relationship between hypercholesterolemia and gallstone formation, it was necessary first to determine whether the level of cholesterol in the blood had any influence on the amount of cholesterol in the bile. Since it is recognized that changes in the blood cholesterol occur in hyperthyroidism and hypothyroidism and because these conditions can be experimentally produced in animals, it was decided to study the cholesterol in the blood and hepatic bile of biliary fistula dogs during the experimental production of these conditions.

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## EXPERIMENTAL

Normal dogs on the routine animal house diet were used in these experiments. Biliary fistulas were prepared by cholecystectomy and double intubation of the common duct by a method previously described.<sup>9</sup> With this method, samples of hepatic bile could be collected when desired, or the two tubes could be connected and the bile allowed to flow into the duodenum. The operations and aftercare of the wounds were done with due regard to aseptic precautions. The animals were divided into four groups:

1. Four animals served as controls. These received no further treatment. Bile was collected at intervals and analyzed for cholesterol concentration.

2. The second group consisted of four dogs to which desiccated thyroid extract was fed. The dose varied from 10 to 30 gm. a day. The total dosage varied from 300 to 550 gm. At intervals, the blood cholesterol was estimated and twenty-four-hour bile samples were collected for cholesterol determinations.

3. In the third group four dogs were given from 50 to 90 mg. of thyroxin\* intravenously over a period of from five to ten days. Cholesterol analyses of the blood and bile were made at intervals during the experiment.

4. In the fourth group four dogs were subjected to a total thyroidectomy in addition to the biliary tract operation. In two of the dogs the total thyroidectomy was performed after the biliary fistula was established, while in the other dogs the thyroidectomy was performed about three weeks before cholecystectomy and double intubation of the common duct. Here, again, blood samples and twenty-four-hour bile samples were analyzed for cholesterol.

The cholesterol determinations were made by the colorimetric method of Autenrieth and Funk, as described by McMaster.<sup>10</sup>

## RESULTS

In Fig. 1 are shown the hepatic bile cholesterol concentrations and total twenty-four-hour output at intervals on four normal dogs. The cholesterol varied from 4.6 mg. per 100 c.c. to 56 mg. per 100 c.c.; while the total twenty-four-hour output varied from 5 mg. to 54 mg.

Fig. 2 shows the results of feeding four dogs desiccated thyroid for considerable periods of time. There was no change in the bile cholesterol that could be attributed to the thyroid feeding. It will be seen that, although the blood cholesterol fell considerably as the result of the thyroid feeding, there was no significant change in the cholesterol concentration, or total cholesterol output in the bile, the variation being approximately the same as in the group of control dogs.

\*The thyroxin used in these experiments was kindly furnished by Eli Lilly and Company.



50 mg. of the thyroxin intravenously and were probably thyrotoxic. Examination of the bile cholesterol concentrations reveals no significant variation from the controls as the result of thyroxin administration.

In Fig. 4 are shown the results of the efforts to produce hypothyroidism. In Dog 655 the blood cholesterol concentration rose to 363 mg. per cent. In none of the dogs was there a significant variation in the bile cholesterol concentration from the normal values.

#3.

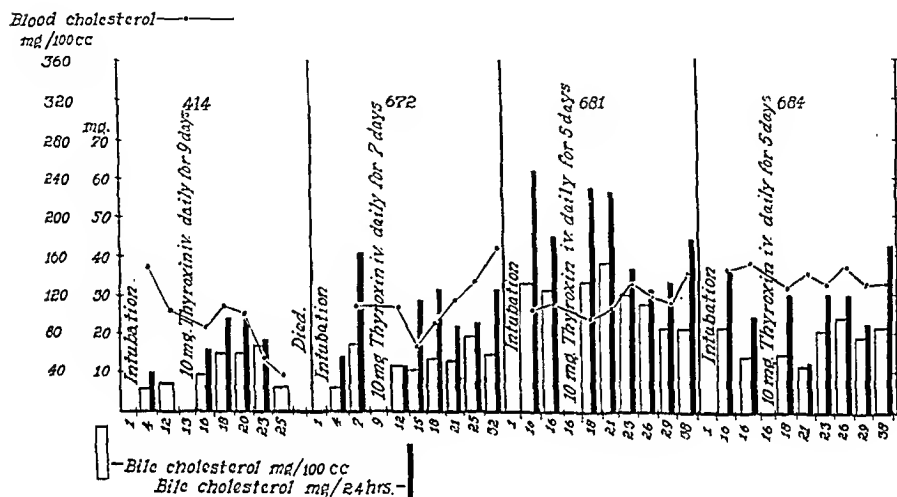
*Dogs Given Thyroxin Intravenously.*

Fig. 3.

#4

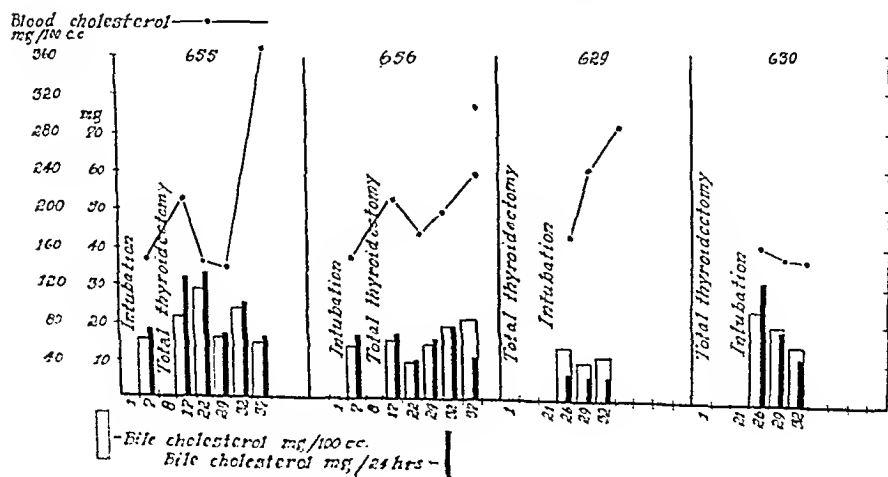
*Dogs Having Total Thyroidectomy.*

FIG. 4.

## DISCUSSION

It is obvious from the data in Fig. 1 that the variation in cholesterol concentration in the hepatic bile of the normal dogs is considerable. Such variations have also been reported by McMaster.<sup>10</sup> Any change in the bile cholesterol produced by our experimental methods, therefore, would have to be constant and considerable to be significant. We would consider that, if after the administration of thyroxin or after total thyroidectomy, the bile cholesterol concentration or total bile cholesterol output reached either a high or low value and remained so throughout the experimental periods, the effect could be attributed to the experimental condition and, therefore, would be significant. If, however, the bile cholesterol continued to show the same daily variations at approximately the same level as in the normal animals, it could be assumed that the variations in the blood cholesterol concentrations were without effect on the bile cholesterol concentration under the conditions of our experiment.

It may be questioned, of course, whether the animals used in these experiments were hyper- or hypothyroid. It has been previously demonstrated that hyperthyroidism<sup>11</sup> and hypothyroidism<sup>12</sup> may be produced experimentally by the methods used in these experiments, and the collateral picture in these animals suggested that such states were produced. No basal metabolic rate determinations were made, since we were interested in the relationship between the blood and bile cholesterol concentrations and used the hyper- and hypothyroid states to produce the conditions we desired.

Only a few papers have been published concerning the relationship of the thyroid to bile cholesterol, but, even so, the data are conflicting. Wilkinson<sup>13</sup> and Hurxthal and Hunt<sup>14</sup> reported findings on bile from human patients, indicating that in hyperthyroidism and hypothyroidism the bile cholesterol concentration varies inversely with the blood cholesterol concentration. Unfortunately their figures for bile cholesterol, except in a single instance, are based on the analysis of material obtained by duodenal drainage and in that instance it was not stated whether the bile was obtained from a common duct or gall-bladder fistula. Analyses of duodenal contents for cholesterol, of course, do not give an accurate idea of the amount or concentration of cholesterol in the hepatic bile.

Leites and Isabolinskaja,<sup>15</sup> however, working with dogs with gall-bladder fistulas, reported an increased cholesterol concentration in bile after an injection of 1 mg. of thyroxin subcutaneously. On the other hand, Besuglow and Tutkewitsch,<sup>16</sup> using the same experimental method, reported a fall in the cholesterol concentration of the bile after the injection of 2 mg. of thyroxin and a rise after total thyroidectomy. Blood

cholesterol determinations were not made in these experiments. Parhon and Werner<sup>17</sup> reported findings similar to those of Besuglow and Tutkewitseh, but did not give the method used.

In our experiments we were unable to demonstrate any significant variation in the concentration or total amount of cholesterol in the bile, with alterations in blood cholesterol produced by experimental hyper- or hypothyroidism. This is in agreement with other experiments carried out in this laboratory<sup>7</sup> in which cholesterol was fed to patients in amounts sufficient to raise the blood cholesterol without having any appreciable effect on the concentration of cholesterol in the bile. It was previously determined that the bile contained sufficient bile salts to maintain the cholesterol in its normal state.

In considering the relationship of the blood and hepatic bile cholesterol concentrations, it should be borne in mind that while the cholesterol in the blood is found in both the free and combined states, the bile under normal conditions contains only free cholesterol. It was possible, therefore, that a relationship may have existed between the free cholesterol of the blood and that of the bile. In four experiments in which the free and combined cholesterol of the blood, and the free cholesterol of the bile were determined, we found no evidence of such a relationship.

#### SUMMARY

1. When dogs were given large doses of desiccated thyroid by mouth or large doses of thyroxin intravenously, there was no demonstrable effect on the cholesterol concentration, or the total cholesterol output of the hepatic bile, although the blood cholesterol fell as low as 40 mg. per cent.

2. When total thyroidectomy was done on dogs there was no demonstrable effect on the cholesterol concentration or the total cholesterol output of the hepatic bile, although the blood cholesterol rose as high as 363 mg. per cent.

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# ETIOLOGICAL FACTORS IN ACUTE APPENDICITIS

## BASED UPON A STUDY OF 3,400 CASES

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FIFTY-TWO years have now passed since the pathologist Reginald Fitz<sup>7</sup> firmly established appendicitis as a definite clinical entity. Since then one would naturally assume that the morbidity and the mortality of appendicitis would have markedly decreased. However, the opposite status has been the strange result here in the United States.

Today the incidence of appendicitis is approximately fifteen times that recorded for the year 1885.<sup>3</sup> The mortality of acute appendicitis has increased 34 per cent in the last quarter of a century. Thus, despite the remarkable advances made in other fields of both medicine and surgery, appendicitis has remained unconquered and its ravages are largely unchecked. It is estimated that now 20,000 persons<sup>1</sup> die from this disease yearly in the United States. When this high death rate is compared to the markedly lowered incidence of appendicitis existent elsewhere throughout the world, it is apparent that continued study on this problem is necessary, in an effort to halt this needless waste of valuable young human life.

The recent contributions of Nicholson,<sup>9</sup> Wangensteen and Bowers,<sup>12</sup> Wangensteen, Buirge, Dennis, and Ritchie,<sup>13</sup> Bowen,<sup>3</sup> Spencer,<sup>11</sup> Wood,<sup>14</sup> Archibald,<sup>2</sup> Robertson,<sup>10</sup> Brown,<sup>6</sup> Bower, Burns, and Mengle,<sup>4, 5</sup> and Nicholls<sup>8</sup> have been of great importance in presenting a clearer conception of the many features of appendicitis. We have been interested, for some time, in the problem of the etiology of acute appendicitis. Recently, our cases have been reviewed from this viewpoint; 3,400 cases of proved acute appendicitis have been studied. The report of the surgeon concerning his operative findings, the pathologist's study of the specimen, and the patient's history were carefully reviewed for data in reference to etiological factors in the causation of that particular instance of acute appendicitis.

There were 2,011 males (59.1234 per cent). The average age of this series was 23.48 years. The aggregate uncorrected mortality was 3.5574 per cent, or 121 deaths. This series was divided into the three following classifications, as recently used by Wangensteen:<sup>12</sup> acute suppurative appendicitis, 1,901 instances (55.8894 per cent); nonperforative gan-

TABLE I  
TABULATION OF THE DEATHS IN THIS SERIES

DEATHS (121 CASES)	ACUTE SUPPURATIVE APPENDICITIS (1,901 CASES)	NONPERFORATIVE GANGRENOUS APPENDICITIS (1,108 CASES)	PERFORATIVE GANGRENOUS APPENDICITIS (391 CASES)
Number	17	51	53
Percentage of 3,400 cases	0.4998	1.4994	1.5582
Percentage of all deaths	14.0488	42.1464	43.7992
Percentage of cases in each group	0.89403	4.60275	13.5521
Sex: Males	12	38	33
Females	5	13	20
Average age of those dying, in years	20.94	23.03	29.16

grenous appendicitis, 1,108 examples (32.5752 per cent); and perforative gangrenous appendicitis, 391 patients (11.4954 per cent).

A study of Tables I and II shows that fecaliths and appendicoliths appear to play a major role in the etiology of both the uncomplicated gangrenous and perforative types of appendicitis. Lymphoid hyperplasia, stenosis, and kinks in the lumen are likewise important etiological factors. Evidence derived from this study showed that appendicitis resulting from enterogenous infection was not uncommon. Foreign bodies and parasites in the appendiceal lumen assumed little significance in this group of cases. The hematogenous origin of acute appendicitis was likewise of minor importance. The etiology of 55.43 per cent of the instances of acute suppurative appendicitis has remained undetermined. The same statement is true concerning 34.81 per cent of all the cases in this entire series.

#### SUMMARY

The etiological factors in 3,400 consecutive unselected instances of proved acute appendicitis have been briefly indicated. This study demonstrated that fecaliths and concretions in the lumen are the most common etiological factors (30.2326 per cent) of severe acute appendicitis; 20.6388 per cent of this series showed either hypertrophy of the lymphoid follicles, stenosis, or kinks of the appendiceal lumen. These also acted as definite obstructive lesions; 10.4546 per cent of the entire series were believed derived from an enterogenous origin; 1.4582 per cent of the appendices contained foreign bodies in the lumen. Obstructive factors in 50.8714 per cent of this series of acute appendicitis were considered primarily responsible for the acute inflammation. Foreign bodies and parasites in the lumen constituted an additional 2.5520 per cent of this entire group. Obstruction of the appendiceal lumen was responsible for 81.2240 per cent of the examples of acute gangrenous appendicitis, while the same factor caused 79.6341 per cent of the instances of perforative gangrenous appendicitis.

TABLE II  
ETIOLOGICAL FACTORS IN THE CAUSATION OF ACUTE APPENDICITIS  
(NUMBER AND PERCENTAGE OF EACH TYPE)

	LUMEN FECALITH AND APPENDICO- LITHS	HYPERTROPHY OF LYMPHOID FOLLICLES, AND STENOSIS, AND KINKS IN LUMEN	FOREIGN BODIES IN THE LUMEN	PARASITES IN THE LUMEN	ENTEROGENOUS ORIGIN	HEMATOGENOUS ORIGIN	CAUSE IS UNKNOWN
Acute suppurative appendicitis (1,901 Cases)	173 9.04548%	346 18.20014%	39 2.05101%	14 0.7362%	249 13.0949%	27 1.4109%	1,054 55.42986%
Nonperforative gangrenous appendicitis (1,108 Cases)	653 58.93225%	247 22.29175%	11 0.99275%	8 0.7220%	103 9.2957%	12 1.0830%	74 6.67850%
Perforative gangrenous appendicitis (391 Cases)	204 52.1628%	109 27.4713%	3 0.7671%	5 1.2785%	7 1.7899%	7 1.7899%	56 14.3192%
Total cases	1,029	702	53	27	359	46	1,184
Percentage of 3,400 Cases	30.2326	20.6388	1.4582	0.7938	10.4546	1.3524	34.8096

## CONCLUSIONS

1. Obstructive factors assume the major rôle in the causation of acute appendicitis.
2. Appendiceal fecaliths and concretions are the most common acute obstructing agent encountered in the two subgroups of this series where 85.9456 per cent of the deaths occurred.
3. The clinical recognition of these obstructing factors will promote better treatment in acute appendicitis.

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## CIRCUMCISION

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CIRCUMCISION is a procedure of great antiquity. It has been associated with religious or hygienic rites of many ancient races. While historic reviews are of great interest, the indications for circumcision have changed little during the years.

From a purely urologic viewpoint, we are concerned with the question of infections and obstructions as engendered by a phimosis or a redundant foreskin. In addition to the conditions mentioned above, we have the relationship of phimosis to penile cancer. Wolbarst and Dean agree that there are no recorded cases of epithelioma of the glans penis occurring in a person circumcised in infancy. Dean states the prophylaxis of cancer of the penis is circumcision of all male infants shortly after birth.

The literature is replete with descriptions and comments on circumcision and devices for performing it. Borey, in 1907, presented a very ingenious phimosis clamp. Lewis, in 1914, described a device for this operation, which, differing somewhat in design, was based on similar principles.

In a previous communication (1935) a preliminary report was made of a technique for circumcision in the adult. Since the presentation of 10 cases two years ago, 51 additional personal patients have been operated upon and data obtained by questionnaire on 102 more. The method has been so satisfactory in our hands that a survey of the technique at this time seems warranted.

It is a simple operative procedure which can be readily carried out in the office. The following items are necessary: procaine 2 per cent (with vasoconstrictor), 27 gauge needle, 4 small hemostats, scissors, knife, probe, thumb forceps, needle holder, a piece of No. 25 gauge annealed copper wire, No. 00 plain catgut suture with atraumatic needle, and a proper size circumcision clamp. The clamp consists of 4 parts (Fig. 1): a cone (Fig. 1a), a base plate, a top plate, and a screw. The method of its application is described below.

The action of the clamp (Fig. 1d) is dependent upon pressure being exercised upon a very narrow rim of tissue which insures adherence of the outer skin and the inner preputial surface. With that accomplished, it permits removal of the redundant tissue and temporarily prevents retraction of the blood vessels. It is, of course, necessary to have a cone which properly fits the glans. This can be determined by a trial fitting

prior to the procedure. In the personal cases cited above, 6 required a clamp with the base diameter of 3.2 cm.; 52, with a diameter of 2.9 cm.; and 4, with a diameter of 2.6 cm.

With the patient on the examining table, the penis is prepared and draped in the usual manner. Hertzler's method of local anesthesia has been found the most satisfactory. Usually 3 to 5 c.c. of procaine are sufficient for the operation. A circular subcutaneous injection is made about midshaft (Fig. 2a); 1.5 to 2.5 c.c. are adequate. Following this, the fore-

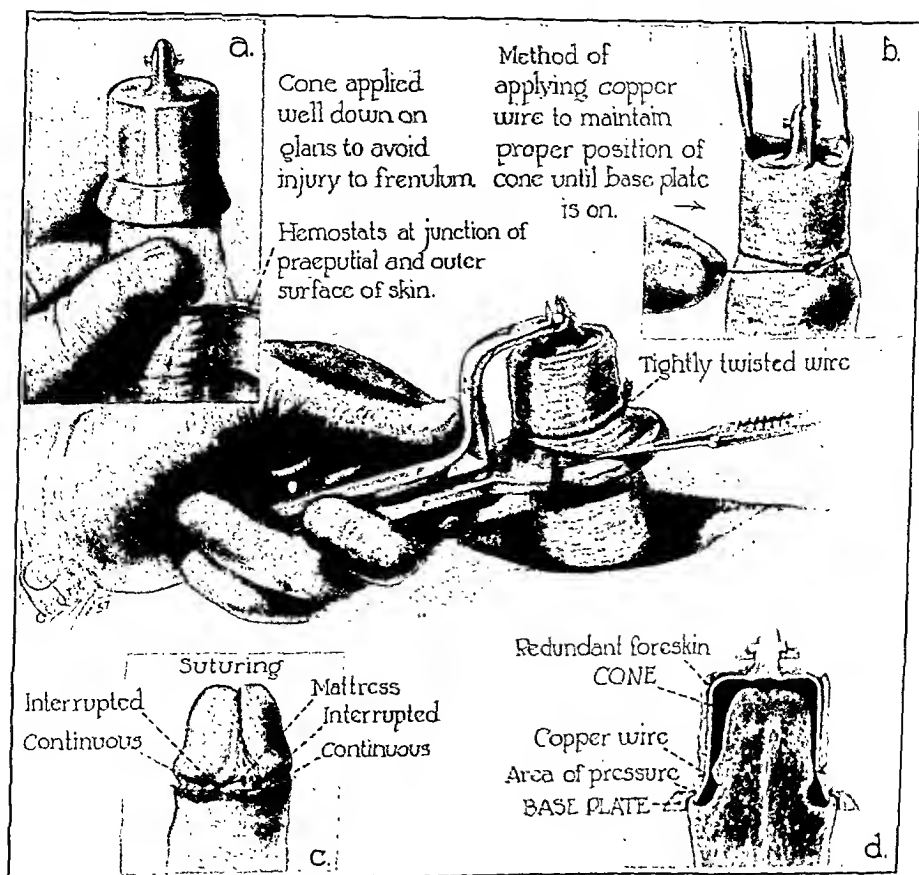


FIG. 1.

skin is retracted and a series of injections are made about the corona. The solution is forced toward the base of the glans (Fig. 2b). Considerable care should be exercised to prevent distortion of the tissue. The anesthetic ring must completely encircle the glans and the frenulum should be also infiltrated. Usually 1.5 to 2.5 c.c. are ample.

If the foreskin is not retractile, a line of infiltration is made dorsally and a slit, just long enough to allow complete retraction, is made; then the coronal infiltration described above may be done. All adhesions are

freed. The redundant tissue is grasped by hemostats at the junction of the skin and mucosa and then retracted. The cone, which has been lubricated on its inner surface with a little vaseline, is slipped over the glans (Fig. 1a). The mass of tissue is then pulled over the cone. Tension on the hemostats and counter pressure on the cone permit almost any amount of tissue to be removed. However, care in applying the cone is necessary since this prevents any injury to the frenulum. Next, a piece of copper wire is twisted about the redundant tissue to maintain its relationship to the cone (Fig. 1b). The hemostats are removed and the base plate is slipped over this mass. The top plate is then hooked under the arms of the cone and slipped into its notch in the base plate and the screw is turned down until it is tight.

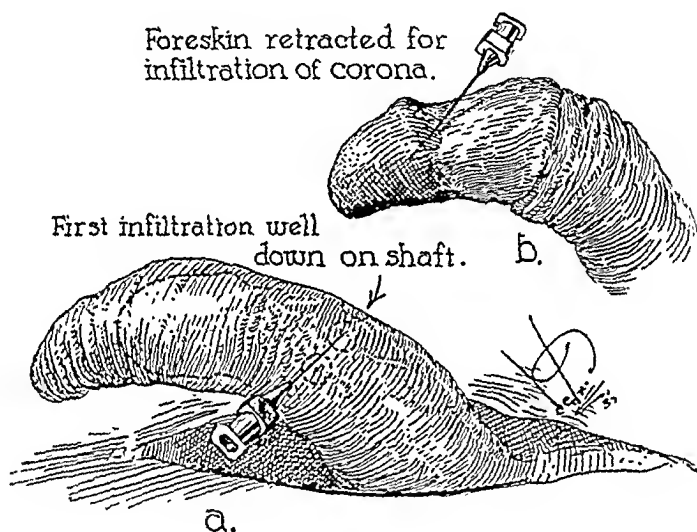


FIG. 2.

At the end of five minutes, the redundant tissue is removed by holding the knife parallel to the base plate and cutting about its circumference (Fig. 1c). The instrument is then loosened and removed. This pressure has given temporary coaptation of the cut edges and hemostasis. Since neither of these is permanent, considerable care is necessary in suturing. The first step is a mattress at the frenulum (Fig. 1c). Next, two interrupted sutures are placed on either side of this, to complete and maintain the triangle at the frenulum; then a mattress suture is placed dorsally. A simple running suture on either side with rather closely placed stitches completes the procedure.

## COMMENT

It is evident that considerable care should be exercised in suturing; any large vessels that can be seen should have a mattress suture placed about them. With care in this step, the operation is practically bloodless.



The sutures usually drop out on the fifth day and the wound is sealed in a week. Simple daily dressings are done. No unusual complications or sequelae have been observed or reported.

#### NOTES ON INFANT CIRCUMCISION

The technique for infant circumcision was devised by Yellen, who reported 500 cases. I have been able to collect records on 300 additional infant circumcisions. There were no complications noted in this series of 800 cases.

The method is essentially the same as in the adult. There are a few precautions which must be carefully noted.

All adhesions must be dissected free before applying the clamp. Ordinarily, stretching of the prepuce will permit retraction for the dissection; if it does not, a dorsal slit is done. The slit should not be too long, however, since difficulty in keeping the cone in place will be encountered with a deep slit. Only a clamp of the proper size should be used.

No sutures or anesthesia are required in the newborn. In older children a few interrupted sutures suffice.

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# Editorial

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## The Dressing of Infected Wounds

THOSE of us making regular rounds in the wards of large municipal hospitals are struck with the variety of means and methods of the dressing of infected wounds by our resident staff officers. This striking difference in technique employed reflects not only the teaching they have been exposed to but their desire to try various recommended methods. These vary from irrigations and application of various solutions, often highly colored, to adhesive strips neatly latticed across the granulation tissue. The results of the treatment are frequently as varied as the methods.

In 1917 it was my very good fortune to be assigned for a short time to the Rockefeller Institute for a course given for the study of the use of Dakin's solution. One of the outstanding impressions of the course was the meticulous care in which infected wounds were prepared before the treatment by Dakin's solution. The skin was carefully shaved for a distance of three inches around the wound. By the use of sterile soap and water on sterile sponges held on sterile instruments, the skin was gently but carefully and thoroughly washed so that dried pus, blood, scales of skin, or other foreign material was entirely removed from the environment of the wound. This was called the mechanical treatment of the wound.

In 1918 and 1919 in France, almost all of the hospitals were swamped with work and we found ours no exception, so that the time-consuming details of the use of Dakin's solution were confined to a few wards. In the remaining major portion of the wards we decided to use the so-called mechanical treatment of infected wounds. Food carts were converted into dressing carts on which were carried sterile instruments, sterile soap and water, and sterile sponges, in addition to the other necessities. The dressings were lifted off the wound by instruments. Several light scrubbing with small sponges soaked in sterile soap solution followed. Scabs, scales, pus, and blood disappeared, and a sterile dressing was applied without touching the wound with the fingers. The net result of this treatment showed the same improvement in the appearance of the granulation tissue as in the wounds in which Dakin's solution was also used; just as many delayed closures were possible and just as many wounds became as quickly suitable for skin grafting.

Since the War this same technique has been used in our ward at the Cook County Hospital with great satisfaction. The principles are obvi-

The sutures usually drop out on the fifth day and the wound is sealed in a week. Simple daily dressings are done. No unusual complications or sequelae have been observed or reported.

#### NOTES ON INFANT CIRCUMCISION

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The method is essentially the same as in the adult. There are a few precautions which must be carefully noted.

All adhesions must be dissected free before applying the clamp. Ordinarily, stretching of the prepucce will permit retraction for the dissection; if it does not, a dorsal slit is done. The slit should not be too long, however, since difficulty in keeping the cone in place will be encountered with a deep slit. Only a clamp of the proper size should be used.

No sutures or anesthesia are required in the newborn. In older children a few interrupted sutures suffice.

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# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## REGIONAL ENTERITIS

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**B**ENIGN or nonspecific enteritis or ileitis, localized chronic cicatrizing enteritis, infectious or nonspecific granuloma of the ileum, regional ileitis or enteritis are terms variously applied to the clinical entity, terminal ileitis, first described as such by Crohn, Ginzburg, and Oppenheimer<sup>1</sup> in 1932. Regional enteritis is now favored as the more inclusive term in view of the broadening interpretation of this disease.

The present concept of regional enteritis differs from that of terminal ileitis as described by Crohn and his co-workers<sup>1, 2</sup> only in the magnitude of the intestinal involvement. In their original paper, the disease was described as a benign, subacute or chronic necrotizing and cicatrizing inflammation of unknown origin attacking only the terminal portion of ileum and usually appearing among young adults. The reaction in the ileum results in ulceration of the mucosa, fibrotic invasion and hypertrophy of the muscularis and mesentery which frequently progresses to stenosis of the intestinal lumen and to the formation of multiple fistulas and adhesions. That portions of the small intestine proximal to the terminal part of the ileum might be affected by an identical process was substantiated in 1933 by Harris, Bell, and Brunn<sup>3</sup> who reported a case in which the jejunum was diseased. The following year Brown, Bergen, and Weber<sup>4</sup> observed that the colon adjacent to the involved terminal portion of ileum could be invaded by extension of the process to segments distal to the ileocecal valve. Since 1934, many authors have reported this same finding. Crohn himself favored the view in a more recent report.<sup>5</sup>

Since early in the nineteenth century, references<sup>6-8</sup> have appeared in the literature which attest the recognition of a benign lesion in the small intestine producing stricture, obstruction, abscess, and fistula. These cases were overlooked, except that they were classified with that ill-defined group designated "granuloma of the intestine" which included all benign tumors and did not exclude the specific granulomas caused by tuberculosis, syphilis, and so forth; in fact, many of the lesions were

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ous and the materials are cheap. If the skin surrounding an infected wound is treated as if it were potentially a sterile field, the wound itself is spared contamination by shifting dressings. The granulation tissue contains most of the fighting forces of the body against infection. Left to its own devices and protected from constant recontamination, it soon demonstrates its ability to combat the infection upon it. The result is a wound covered with a red, healthy bed of granulation tissue, with all evidences of healing.

We believe it should be constantly pointed out to our resident staff that the applications of strong antiseptic solutions on granulation tissue have no power to penetrate the granulation tissue to reach infectious bacteria without at the same time injuring or destroying granulation tissue, which after all is the white hope in wound healing.

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studied at the clinic, Pumphrey<sup>15</sup> has followed every clue or suggestion of other authors and of the bacteriologic department of the clinic, but he was not successful in discovering the etiologic factor in this disease. His findings have been published elsewhere.

None of the aforementioned possible factors accompanied regional enteritis frequently and in those instances in which there was such an association it seemed coincidental.

Felsen<sup>16</sup> is the only one who unequivocally stated that *Bacillus dysenteriae* is the etiologic factor. Mixer<sup>17</sup> reported isolation of an anaerobic streptococcus from a macerated mesenteric lymph node removed from one of his patients. He also suggested the possibility of a racial predilection because of the high percentage of Jews in one reported series of cases.

Jackson<sup>18</sup> held the view expressed previously by Bargen and Dixon<sup>19</sup> that there is a relationship between mesenteric lymphadenitis and terminal ileitis and that both lesions are due to disease of the lymphatic system in the region involved. Probst and Gruenfeld<sup>20</sup> likewise felt that the lymphatic vessels in the affected site are in some way responsible and these authors expressed the view that stagnation and great abundance of lymphatic tissue in the region account for the frequency of attacks on the terminal portion of ileum. Certain it is that when the bacterial flora of the fecal current reaches the ileocecal valve, it has acquired its maximal degree of infectiousness and toxicity.<sup>21</sup> The experimental work of Reichert and Mathes<sup>22</sup> is of interest concerning this point. They injected irritating and sclerosing materials into the mesenteric and subserous lymphatic vessels and this brought about chronic lymphedema of the intestinal wall. They believed that infection of low grade and concomitant chronic lymphedema are the two dominant features.

W. J. Mayo<sup>23</sup> in a personal communication to the authors suggested the possibility of some acid-fast variant being responsible. He recalled encountering conditions early in his career like those described in modern literature under the term "regional enteritis." At that same time there were many cases of serofula and tuberculous peritonitis. With the elimination of the source of avian and bovine tuberculosis, all of these entities became rare. In this connection it is to be remembered that in instances of Johne's disease of cattle the small intestine is involved in a process similar to that of regional enteritis and a pseudotubercle bacillus is the etiologic agent.<sup>24, 25</sup> Felsen and Pumphrey are now conducting investigations which should settle this question definitely.

Although the hypothesis that some allergic phenomena are responsible has been advocated, most investigators feel positive that the origin of this disease is bacterial. Its close resemblance to lymphogranuloma inguinale, both in the stage of early involvement of the regional lymph

considered tuberculous. Braun<sup>9</sup> reported an inflammatory tumor of the sigmoid flexure in 1908. Tietze,<sup>10</sup> in 1920, thoroughly reviewed the literature on benign granuloma up to that time. Mosehcowitz and Wilensky,<sup>11</sup> in 1923, reported 4 cases, in 3 of which the colon was involved and in 1 of which the terminal ileum was attacked. In 1931, Moek<sup>12</sup> presented a very comprehensive article dealing with all types of nonspecific inflammatory tumors, principally of the colon, and he definitely established the fact that the specific granulomatous lesions of tuberculosis, syphilis, pathogenic fungi, parasites, and lymphosarcoma were not to be included in the classification. However, the introduction of new concepts regarding regional ileitis and its designation as a distinct clinical entity was the accomplishment of Crohn and his co-workers. Since their report in 1932, more than 100 articles have been published representing reports of more than 500 cases. In a recent survey, Lick<sup>13</sup> reviewed all of the literature in a very comprehensive manner. Certainly the disease is receiving greater recognition than formerly although the question of an increase in its incidence is still debatable. From January, 1922, to September, 1936, 39 proved cases of regional enteritis were encountered at the Mayo Clinic<sup>14</sup> and in the next two years 44 patients have submitted to operation for the same condition. The data used in this paper are derived from the study of these 44 cases.

Very little has been learned about the disease since the time when the first case was reported. Its etiology remains unknown and the ideal form of treatment is yet to be established. Recording of additional cases is useful pending development of a specific plan of treatment.

#### ETIOLOGY

Numerous observers have suggested possibilities as to the cause of this inflammatory involvement of the intestine, but careful perusal of their studies and even intensive investigation leads one to the conclusion that the etiology remains a matter of conjecture. All patients who come to the Mayo Clinic and who have regional enteritis are subjected to the following investigations preoperatively: (1) The stools are examined for Bagen's diplostreptococcus, for the bacteria which produce dysentery, for *Mycobacterium tuberculosis*, ova, parasites, amoebae, blood, and pus. (2) The blood is tested for the presence of syphilis and for evidence of the various dyscrasias and agglutination tests are conducted against the groups of intestinal bacteria, undulant fever, and tularemia. (3) Intradermal tests for tuberculosis (Mantoux) and lymphopathia venereum (Frei) are performed. (4) Roentgenologic studies of the thorax are made to eliminate the possibility that tuberculosis is present. (5) If fecal fistula is present, the pus and scrapings of the tissue are investigated for evidence of actinomyces, blastomycosis, and tuberculosis. Postoperatively, extensive bacteriologic and pathologic studies are made of the bowel, mesentery, and lymph nodes. In the last twenty cases

most, the formation of a small, walled-off abscess which sometimes discharges its contents into an adjacent viscus. For instance, the terminal part of the ileum may be found to communicate with the bladder, as in a case in which small sinuses led to these organs from a thick-walled abscess having a capacity of about 2 ounces. In addition, fistulous communications between the diseased portion of bowel and the abdominal parietes were present in 8 cases. Intraintestinal communications were present in an equal number of cases, but did not produce symptoms. These small tracts connected a coil of involved ileum and an adherent segment of adjacent bowel, usually the ascending portion of colon, the ileum, or the sigmoid flexure. In 3 instances in this series the sigmoid flexure was perforated.

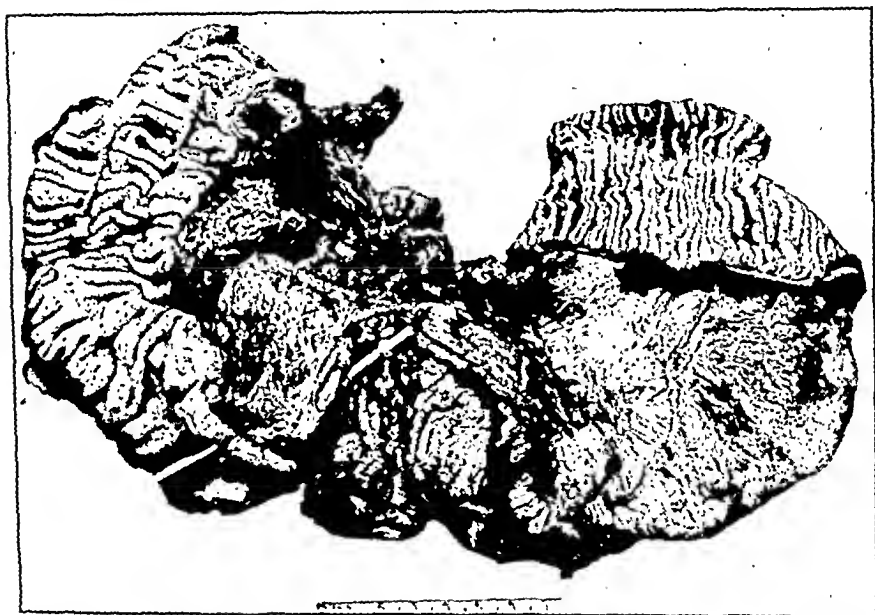


Fig. 1.—Regional enteritis involving terminal portion of the ileum and the cecum, showing the severe hyperplastic type of inflammatory process.

The distal portion of the ileum appeared to be the original site of invasion of the disease in practically all cases. The affected segment is readily discovered on opening the abdomen. According to our observations the most striking gross features are the typical enlargement and loss of flexibility of the affected segment of bowel and the shortened and greatly thickened mesentery in which the regional lymph nodes are large and firm. The tissues have a dusky, bluish-red appearance and a phlegmonous exudate is distributed sparingly over the serosal covering of the intestine.

If obstruction is pronounced, the portion of intestine just proximal to the site of the disease may be extremely dilated and the muscular elements may be hypertrophic. In the instances in which the condition



nodes and in the subsequent stage of severe cicatricial stenosis of the affected portion of bowel would suggest the same type of causative agent; that is, a filtrable virus.

### PATHOLOGIC MANIFESTATIONS

The gross and microscopie appearance of the specimens obtained at resection showed the process to be that generally attributed to inflammatory invasion. However, since the disease is of progressive nature, the exact findings depend on the phase in which the operation is performed. Generally speaking, the patients observed at the clinic are in the advanced stages of the disease and the pathologic process has produced unmistakable gross deformity resulting from fibrotic repair after chronic inflammation on which acute exacerbations of the disease have been superimposed. The early phases of the disease are not yet sufficiently well known to prevent the performance of simple appendectomy when resection or a side-tracking procedure would be the more suitable operation.

Descriptions of the pathologic process show striking uniformity. Although the terminal portion of ileum is the segment most frequently involved, no part of the intestinal tract is exempt (Table I). In 20 of

TABLE I  
REGIONAL ENTERITIS: SITE OF PATHOLOGIC PROCESS IN 44 CASES

SITUATION	NUMBER OF CASES
Ileum	20
Jejunum and ileum	1
Jejunum, ileum, and cecum	1
Ileum and cecum	14
Cecum	1
Ileum, cecum, and ascending colon	2
Ileum, cecum, ascending and transverse colon	2
Ileum, cecum, ascending, transverse, and descending colon	2
Ileum, cecum, transverse colon, and sigmoid flexure	1

the 44 cases in this series the ileum alone was affected. The jejunum was not attacked solely in any of the cases, but in 1 instance the jejunum and ileum were involved and in another the jejunum, ileum, and cecum were invaded. The ileum and cecum were the site of the disease in 14 cases (Fig. 1); the ileum, cecum, and ascending portion of the colon, in 2; the ileum and the ascending, transverse, and descending portions of the colon, in 2; and the ileum and the ascending and transverse portions of the colon and sigmoid flexure, in 1. The process was confined to the cecum in 1 case.

If an external fistula was present, it was almost invariably the result of an operation in which the diseased portion of bowel was incompletely removed. Internal fistula develops after chronic perforation has occurred. The latter process takes place so slowly that it permits segregation of contaminating materials from the general peritoneal cavity, or, at the

diameter of only a few millimeters by the piling up of fibrotic tissue (Fig. 3). The submucosa and muscularis are greatly thickened, their normal structure being largely replaced by fibrous connective tissue and inflammatory exudate (Fig. 4). The mesentery is very friable and bleeding occurs readily. Furthermore, it is so extensively invaded by



Fig. 3.—Regional enteritis involving the terminal portion of the ileum and the ileocecal valve, with almost complete obstruction at the valve (from same case as shown in Figs. 5 and 61).

the inflammatory process that the attached portion of intestine is likely to be immovable.

Microscopic studies fail to reveal specific characteristics. Evidence of any relationship to tuberculosis, syphilis, actinomycesis, Hodgkin's disease, lymphosarcoma, or other malignant process is not demonstrable. The findings are those of acute, subacute, or chronic hypertrophic exuda-

is of long standing, many exacerbations have occurred and there is evidence of chronic perforation; the terminal ileum and cecum may be bound together in the right iliac fossa, forming a large phlegmonous mass which almost requires chiseling to separate it from the iliac bone and parietal peritoneum. Lying between diseased portions of the intestine there may be segments which are apparently normal.

When the resected specimen is examined, it will be found that the caliber of the lumen of the diseased portion of bowel is greatly reduced due to thickening of the intestinal wall. This loss of elasticity produces

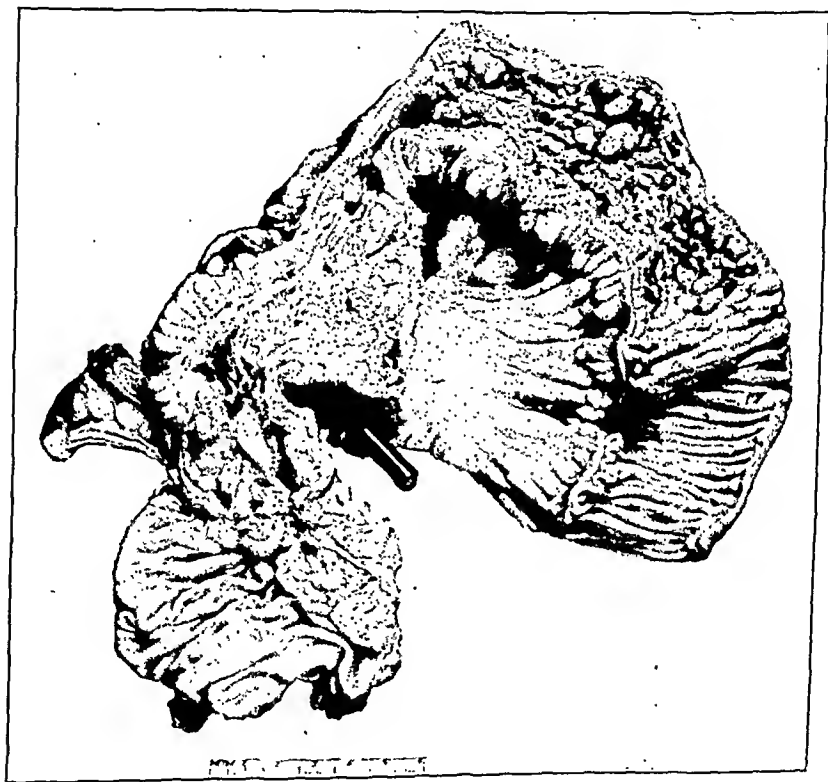


Fig. 2.—Ulceration and destruction of mucous membrane of terminal portion of ileum (from same case as that shown in Fig. 1).

a soggy consistency and hose-like appearance. The mucosa presents a picture varying from that of edema with mild ulcerated regions to almost complete loss of all epithelial structure (Fig. 2). In the typical case the ulcers are found along the mesenteric border and old scars also will be present immediately adjacent to the new regions of ulceration. The intervening mucosa occasionally assumes a pseudopolypoid form. If the terminal portion of ileum is involved, the most advanced pathologic process is generally in the most distal region. The ileocecal valve often will be found entirely obliterated, its lumen being reduced to a

diameter of only a few millimeters by the piling up of fibrotic tissue (Fig. 3). The submucosa and muscularis are greatly thickened, their normal structure being largely replaced by fibrous connective tissue and inflammatory exudate (Fig. 4). The mesentery is very friable and bleeding occurs readily. Furthermore, it is so extensively invaded by



Fig. 3.—Regional enteritis involving the terminal portion of the ileum and the ileocecal valve, with almost complete obstruction at the valve (from same case as shown in Figs. 5 and 6).

the inflammatory process that the attached portion of intestine is likely to be immovable.

Microscopic studies fail to reveal specific characteristics. Evidence of any relationship to tuberculosis, syphilis, actinomyces, Hodgkin's disease, lymphosarcoma, or other malignant process is not demonstrable. The findings are those of acute, subacute, or chronic hypertrophic exuda-

tive and necrotizing inflammation with proliferative or reparative elements (Fig. 5). The cells of the lymphoid series appear to predominate except in the early acute stages. In the usual chronic process, the small lymphocyte, plasma cell, and fibroblastic elements are in ascendency; eosinophiles occasionally are present. Submucous lymphoid follicles are invariably numerous and are enlarged. Giant cells are encountered frequently, but this is by no means a uniform finding. These large multinucleated cells often contain particles of a crystalline or lipid nature which have been accounted for as particles of remnants of food that lodged in the ulcerated mucosa. Focal collections of lymphocytes under



Fig. 4.—Greatly thickened mesentery with enlarged inflammatory nodes. Also narrowing and thickening of intestine (from same case as shown in Fig. 2).

the serosa form tubercle-like irregularities which, with the giant cells, undoubtedly account for the erroneous diagnosis of tuberculosis so frequently made in the past.

In the study of twenty-three operative specimens, Coffey<sup>26</sup> found true tubercles with epithelial reaction, central caseation, and typical giant cells in only three specimens. Roentgenograms of the thorax in these three cases revealed the presence of active tuberculosis and the tubercle bacillus was also isolated from the sputum. In no case in this series were the results of roentgenologic examination of the pulmonary fields positive. Acid-fast staining of the pathologic sections did not reveal the presence of *Mycobacterium tuberculosis* and other bacteria were not

encountered with any appreciable degree of uniformity. In cases in which the appendix could be observed, involvement consisted in peri-appendiceal inflammation which was the result of contiguity, a secondary rather than a primary factor.

#### CLINICAL COURSE

A clinical entity of pathologic origin as described of necessity would vary considerably in its manifestations, depending on the extent and situation of the involved segment of bowel. Generally speaking, there

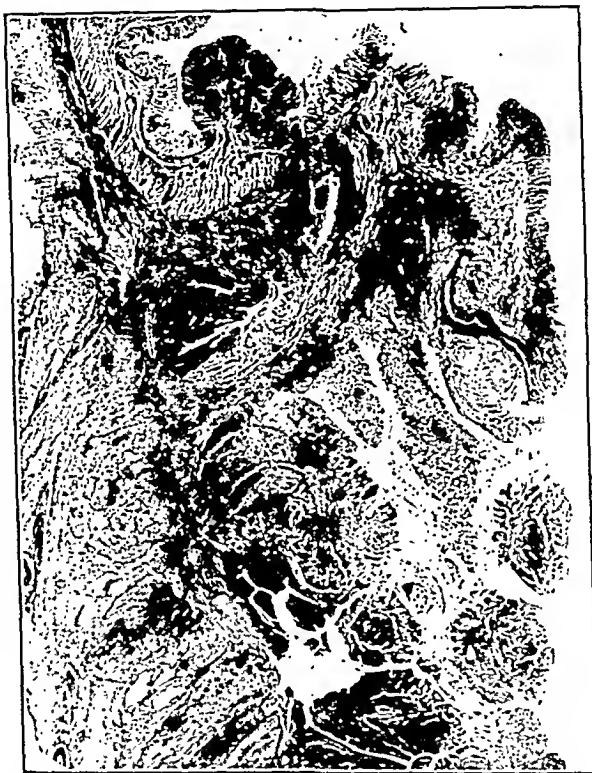


FIG. 5.—Microscopic appearance of specimen taken from ileocecal valve. (From same case as shown in Figs. 3 and 6.)

are four phases through which the disease may pass. The earliest manifestation is that of an acute inflammatory lesion. As the terminal portion of the ileum is the most frequent initial site of the disease, the irritation of this portion of intestine and its adjacent peritoneum produces a picture difficult to distinguish from acute appendicitis. The most frequent symptoms are fever of low grade, leucocytosis, nausea, vomiting, epigastric or right lower quadrant tenderness and pain. Diarrhea and cramps are unusual at this stage of the process. That such symptoms are confusing is attested by the fact that twenty-four of our forty-four patients were subjected to appendectomy prior to coming for treatment

in one of the later phases of regional enteritis. As the disease advances, intermittent attacks of diarrhea are characteristic. This is the stage most frequently confused with chronic ulcerative colitis. The typical syndrome of enteritis of low grade prevails; the patient has fever, anemia, a palpable mass in the right lower abdominal quadrant, and has lost weight; his stools are loose or watery and if any pain is present it is mild and colicky.

Remission of symptoms is frequent in the two stages described, but as the stenosing effect of the disease increases the periods of relief are of shorter duration than before and are less common. The symptoms typical of intestinal obstruction are superimposed on those of chronic enteritis. The attacks of diarrhea are more profound and are accompanied by severe abdominal cramps, borborygmus, abdominal distention, or visible contracture of the coils of the small intestine proximal to the involved segment. Malnutrition and anemia become prominent features since much nourishment and fluids are lost because of the diarrhea; furthermore, intake of food and fluid may be greatly limited on account of persistent nausea or even vomiting.

The fourth and final phase of the disease is attained either when acute obstruction is superimposed on the chronic condition or when perforation of the bowel occurs and formation of an abscess or fistula ensues. As stated previously, the fistula may communicate with an adjacent portion of the intestine or with other viscera or with the abdominal parietes. The debility occasioned by the sepsis and decrease in absorption of nutritional elements and of fluids assumes great significance and in itself may be the important factor in a fatal termination.

The course of regional enteritis as delineated is uniform only in a very general way. In the individual case the first signal of impending trouble may be the onset of the syndrome of the late phases, or the symptomatology may have progressed from that of an occasional episode of pain in the right lower abdominal quadrant or in the epigastrium to that of intestinal occlusion although there has been very little intervening disturbance. In an occasional case, the chief complaint will be one which is only remotely associated with the malady. An instance is recalled in which the terminal part of the ileum was found to be the nidus for infectious arthritis. In another case, peptic ulcer was thought to be responsible for the preprandial pain and profound anemia caused by melena until inflammation and ulceration of the terminal portion of ileum were found through roentgenologic studies.

#### CLINICAL FEATURES

The ages of the 44 patients reported on in this review ranged from 12 to 54 years at the time of onset of the symptoms, although 63 per cent were less than 30 years of age and 84 per cent were less than 40 years of age at the onset of the illness (Tables II and III). The aver-

TABLE II

REGIONAL ENTERITIS: AGES AND DURATION OF SYMPTOMS IN 44 CASES

Average age at onset of symptoms	27.3 yr.
Average age when seen at clinic	31.4 yr.
Maximal age at onset of symptoms	54.0 yr.
Minimal age at onset of symptoms	12.0 yr.
Average duration of symptoms before being seen at clinic	4.1 yr.
Shortest duration of symptoms	4.0 days
Longest duration of symptoms	25.0 yr.

TABLE III

REGIONAL ENTERITIS: AGE INCIDENCE IN 44 CASES

AGE, YEARS	NUMBER OF PATIENTS	
	AT ONSET OF SYMPTOMS	ON ARRIVAL AT CLINIC
Less than 20	6	12
20 to 29	16	16
30 to 39	14	9
40 to 49	2	5
50 to 59	6	2

age age at the beginning of symptoms was 27.3 years. The disturbance had been present for about 4 years before the patients were seen in the clinic. The shortest duration of symptoms was 4 days and the longest was 25 years (Table IV). A third of the patients had been sick less

TABLE IV

REGIONAL ENTERITIS: DURATION OF SYMPTOMS IN 44 CASES

Years	DURATION OF SYMPTOMS, YEARS							
	1 or less	2	3	4	5	5 to 10	10 to 15	20 to 25
Cases	15	7	6	4	2	7	2	1

than 1 year and half of the patients less than 2 years. The course of the disease extended over 10 years in only 3 cases. The average age of the 44 patients when seen at the clinic was 31.4 years. Twenty-four of the 44 patients were males; more than 20 per cent were Jews. Other racial predilections were not noted. The disease has not been observed among Negro patients at the Mayo Clinic.

The chief presenting complaints were: (1) pain, which was not of the cramp-like character associated with diarrhea, in 13 cases; (2) diarrhea in 8 cases; (3) diarrhea and severe abdominal cramps in 13; and (4) fecal fistula in 9. One case did not seem to fit into any of these categories as the only manifestation was a palpable mass in the right lower quadrant of the abdomen.

The pain, other than the cramping pain of the obstructive phase, was of two main types. One type was not dissimilar to the distress of peptic ulcer, being situated principally in the epigastrium. It was dull and intermittent in character and usually was precipitated or was exaggerated by eating and was accompanied by gaseous distention. The other



TABLE V  
REGIONAL ENTERITIS: FREQUENCY OF SIGNS AND SYMPTOMS  
IN 44 CASES

SIGN OR SYMPTOM	NUMBER OF CASES
Loss of weight (average loss, 21.9 pounds)	43
Palpable mass (positive roentgenogram)	32
Diarrhea (average number of stools, 3 to 6)	30
Fever	28
Obstruction	28
Abdominal cramps	25
Anemia	18
Nausea and vomiting	18
Pain other than cramps	12
Blood in stool	7
Fecal fistula	9
Arthritis	3
Tarry stools	1
Appendectomy, on account of symptoms	24
Remission of symptoms	28

type of pain generally occurred in the right lower abdominal quadrant in severe episodes of a few minutes to a few hours' duration and was relieved on occasions by catharsis or by nausea and vomiting. These seizures of pain usually were not accompanied by diarrhea or by cramps although three patients reported an attack of diarrhea.

The diarrhea usually was mild and almost always it was less severe than that accompanying chronic ulcerative colitis. The character of the stool varied from mushy to liquid and, on the average, defecation occurred three to six times in twenty-four hours during a period of activity. One patient reported passing twenty stools in twenty-four hours, which was the maximal number. Generally, gross blood was not passed by rectum, although this did occur in seven of the forty-four cases.

There was usually some cramping pain even in the early stages, although it was not severe. After severe cramping pain began to occur with the attacks, there might be alternating periods of diarrhea and constipation. The diarrhea associated with these intense colicky spasms was of a disturbing nature necessitating frequent evacuation of the bowels, often accompanied by tenesmus. The cramping pain was most severe in the right lower quadrant of the abdomen. It was accompanied by or was relieved by the passage of a loose, watery stool containing mucus and much gas and occasionally by nausea and vomiting. A palpable mass in the right lower quadrant of the abdomen, intestinal obstruction, and severe malnutrition were more frequent among the patients who complained chiefly of abdominal cramps and diarrhea.

Nine patients had external fecal fistulas, one of whom passed feces and gas through the urethra. All of the fistulas developed after the performance of inadequate operative maneuvers in the region of the diseased intestine, most frequently after appendectomy. The fistulas extended from the involved portion of ileum or cecum or from both sites to the right or lower middle region of the abdominal wall. In the case in which

the tract formed a communication between the terminal ileum and the bladder, the sinus had no other external outlet. Four of these nine patients also had intrainestinal fistulas. Fecal drainage from the abdominal fistulas in five cases was profuse and generally the skin surrounding the external stoma was excoriated to the extent that it caused much distress.

The frequency of appearance of various signs and symptoms (Table V) in this group of 44 patients was as follows: loss of weight, 43; palpable abdominal mass, 32; diarrhea, 30; fever, 28; obstruction, 28; abdominal cramps, 25; anemia, 18; nausea and vomiting, 18; pain other than cramps, 12; blood in the stools, 7; fecal fistula, 9; arthritis, 3; and tarry stools, 1. Twenty-eight patients had experienced remissions of their symptoms.

Loss of weight was a characteristic feature of the disease. Each patient had experienced some loss of weight, varying from 2 to 60 pounds; the average loss was 22 pounds.

In the typical case the abdominal mass was found in the lower right side of the abdomen. Usually it was situated rather deeply except among those individuals who had lost much weight, in some of whom the mass was visible as well as palpable. In most instances the mass was firm and dense and did not present the nodular hard consistency characteristic of cancer. It was irregular but smooth, only slightly tender, fairly well fixed, and did not cause reflex rigidity of the abdominal muscles. Distention of loops of bowel may be detected mesial to the mass both by palpation and by visible peristalsis. Occasionally, coils of small intestine are matted together below the brim of the pelvis and can only be felt through the vagina or rectum. In such a case, the differential diagnosis must exclude lesions of the pelvic viscera. The first evidence of an intestinal disorder may consist in detection of a lump in the right side of the abdomen or in embarrassment of the patient from excessive rumbling of gas ("growling").

The blood is practically normal in more than half of the cases. Butt and Watkins<sup>27</sup> have reported the occurrence of a macrocytic anemia in certain instances of terminal ileitis. This anemia did not respond to the administration of the antianemic factor effective in pernicious anemia; however, spontaneous recovery from the anemia occurred following successful extirpation of the diseased segment of bowel. The anemia encountered among eighteen of the patients who had regional ileitis was typically a mild hypochromic anemia, although a severe toxic type of anemia was present in a few cases in which the chief complaint had been severe cramps and diarrhea. The patient whose concentration of hemoglobin was lowest had 9.5 gm. per 100 c.c. of blood; erythrocytes numbered 3,200,000 per cubic millimeter of blood. In the chronic phases of the disease, the number of leucocytes was found to be normal or only

slightly elevated if complications were not present; however, the sedimentation rate of erythrocytes was characteristically increased. The chief features of the other symptoms have been outlined.

#### ROENTGENOLOGIC EXAMINATION AND MANIFESTATIONS

The barium meal and the barium enema are both used as means of investigating the cecum and terminal portion of ileum and each method has



Fig. 6.—After barium meal, showing extreme constriction of lumen of terminal portion of the ileum (from same case as shown in Figs. 3 and 5).

its proponents (Figs. 6 and 7). At the Mayo Clinic, the barium enema is used as the preliminary mode of filling the bowel preparatory to roentgenologic examination. Weber<sup>28, 29</sup> stated that with the contrast enema the coils of the ileum are well elevated out of the pelvis, are distended, and are readily manipulated under roentgenoscopic control by palpation

through the abdominal wall. Furthermore, one must not overlook the danger of filling the proximal part of the intestine with a substance which will pass through the partially obstructed lumen with difficulty. Conversion of partial occlusion into complete obstruction is a conceivable result which may have grave consequences. However, the proximal portion of ileum of necessity must be examined after a contrast meal and



Fig. 7.—After barium enema, showing deformity of cecum and terminal portion of ileum with loss of the mucosal pattern (from same case as shown in Figs. 3 and 5).

therefore the meal is given if a more extensive or confirmatory investigation is desired.

Weber<sup>28, 29</sup> has correlated the roentgenologic manifestations with the presenting pathologic characteristics and has described two general types. His word picture of the conditions found on examination with the contrast media is unsurpassed: "With the hyperplastic character of the

pathologic process in predominance, then the roentgenologic manifestations will be such as are directly or indirectly attributable to hyperplasia. Such changes are narrowing of the lumen due to encroachment on it by the more or less markedly thickened intestinal wall; shortening of the affected segment, due to contraction of the hyperplastic tissue; loss of normal pliability and mobility noted when the diseased intestine is manipulated during the roentgenoscopic examination. With ulcerative features in predominance pathologically, these will be prominent in the roentgenographic picture. Narrowing, shortening and rigidity of the affected segments will not be so manifest, but revealing changes are to be looked for in the pattern of the mucosal relief of the ulcerated segment. Normally, the relief is abundant, but local or general denudation of the internal surface of the intestine is exhibited roentgenologically by a flat, moist, stippled relief which is readily recognized as abnormal. The usual combination is that of hyperplasia and ulceration, with the former predominating. A purely hyperplastic form is only a little more apt to come under observation than a purely ulcerative form. Such complications of this kind of regional enteritis as intra-abdominal and external fistula are demonstrable at roentgenologic examination without great difficulty."

Kantor<sup>30</sup> listed four chief changes in the ileum: (1) a filling defect just proximal to the cecum, (2) abnormality in contour of the last filled loop of ileum, (3) dilation of loops of ileum just proximal to the lesion, and (4) a "string sign" representing the actual lesion.

Thus, the roentgenologic findings are characteristic of the disease. However, they are not pathognomonic because they occur to a certain extent in association with other stenosing lesions of the terminal part of the ileum. The differential roentgenologic diagnosis as regards intestinal neoplasm affords no difficulty with the exception of those lesions which have caused perforation. And even in such cases, careful examination shows the malignant process to be more abruptly demarcated and the mucosal pattern completely eradicated, and on palpation the lesion is hard and knotty owing to induration. Tuberculous enteritis affords the greatest difficulty in diagnosis and it may be a problem for even the most experienced roentgenologist. The general features of both forms of enteritis are much the same. However, Weber<sup>28, 29</sup> has noted that the tuberculous intestine has a rougher and more corrugated appearance than one affected by regional enteritis and the changes correspond to the more irregular development of the ulcerohyperplastic process. Extraintestinal foci of tuberculosis, especially of the lungs, afford the final differential factor. It is conceivable that nonspecific enteritis could occur in the presence of an active tuberculous focus, but we are inclined to classify all such lesions as tuberculous. None of the 44 cases of regional enteritis in this series showed any roentgenologic evidence of pulmonary tuberculosis. The intestinal tract was examined roentgenoscopically in 29 of the cases by use of contrast media. In 5 instances the investigation was omitted

because of the presence of obstruction. The diagnosis of regional enteritis was correct in 36 of the 39 cases. The results of examination of the films in the 3 remaining cases were negative as far as the presence of any such process was concerned.

#### DIAGNOSIS

If the diagnosis of regional enteritis is to be made before operation is undertaken, the symptom complex must be borne in mind constantly. Even then, in an isolated case, the patient may come to operation without a suspicion as to the true nature of the condition having been expressed. In our series of cases an incorrect diagnosis occurred most frequently among those patients who had not experienced symptoms associated with the gastrointestinal tract. The presenting complaint was pain low in the abdomen and on examination a tender pelvic mass could be palpated in the region of the uterine adnexa. An ovarian or tubal abscess was the logical diagnosis. The real cause of the trouble was only determined at the time of operation.

The features of particular importance in making the diagnosis are: (1) acquaintance with the protean manifestations of the disease; (2) presentation of a history suggestive of the ailment which generally includes a report of previous appendectomy, pain, or cramps that have been especially prominent in the right lower quadrant, bouts of mild diarrhea, loss of weight, and fever of low grade; (3) an examination which reveals a mass in the right lower quadrant of the abdomen or evidence of the formation of fistula, emaciation and anemia, scar of a previous appendectomy, evidence of intestinal obstruction, excessive peristalsis, borborygmus, and abdominal distention; (4) roentgenographic evidence of a stenosing lesion of the cecum or of the terminal portion of ileum; and (5) ruling out of all other lesions which, if present, could produce a similar symptom complex.

The roentgenologic findings are by far the most important element in making a definite deduction; in fact, the diagnosis must be largely a matter of conjecture until the definite deformity of the bowel is visualized by the use of contrast media.

Of the conditions that must be considered as a possibility in attempting to make a differential diagnosis, chronic ulcerative colitis probably takes first place; especially is this important because chronic ulcerative colitis is most effectively treated by medical means; whereas, regional enteritis is a surgical problem. Generally, the distinction can be made readily by the use of the sigmoidoscope and barium enema in conjunction with a consideration of the clinical features. However, the diagnosis is more difficult to make in the 5 to 10 per cent of patients who have chronic ulcerative colitis and among whom the ulcerative process involves the proximal portion of the colon and the rectum is normal. Nevertheless, examination with the aid of the barium enema usually will furnish sufficient information on which to make the distinction.

pathologic process in predominance, then the roentgenologic manifestations will be such as are directly or indirectly attributable to hyperplasia. Such changes are narrowing of the lumen due to encroachment on it by the more or less markedly thickened intestinal wall; shortening of the affected segment, due to contraction of the hyperplastic tissue; loss of normal pliability and mobility noted when the diseased intestine is manipulated during the roentgenoscopic examination. With ulcerative features in predominance pathologically, these will be prominent in the roentgenographic picture. Narrowing, shortening and rigidity of the affected segments will not be so manifest, but revealing changes are to be looked for in the pattern of the mucosal relief of the ulcerated segment. Normally, the relief is abundant, but local or general denudation of the internal surface of the intestine is exhibited roentgenologically by a flat, moist, stippled relief which is readily recognized as abnormal. The usual combination is that of hyperplasia and ulceration, with the former predominating. A purely hyperplastic form is only a little more apt to come under observation than a purely ulcerative form. Such complications of this kind of regional enteritis as intra-abdominal and external fistula are demonstrable at roentgenologic examination without great difficulty."

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have had a wide experience. However, the probability that these individuals may later experience a relapse and that the disease will progress to its later stages is something which can be determined only by the lapse of time. Certain it is that among those individuals who have experienced progression of the disease to the extent that there is ulceration, stenosis, malnutrition, obstruction, fistula, or formation of abscess surgical intervention is the only means of combating the irreparable damage to the intestine.

In 32 of the 44 cases here recorded, a preliminary course of medical treatment had been followed for as long as 4.2 years. In the majority the therapy was symptomatic and was given without knowledge of the underlying pathology, but according to the histories of the whole group of patients almost every conceivable mode of attack in the physicians' armamentarium had been given a trial without allaying the inevitable terminal stage. One patient was observed for a period of seven years and during that time underwent three abdominal operations for other conditions. The progress of the intestinal process was observed on an average of every two years and in the interval between operations a medical regimen was carried out with excellent cooperation between physician and patient. At the end of the seventh year and at the time of the third operation it was observed that obstruction of the terminal portion of ileum had become severe, intraileal fistula between the coiled loops of thickened, soggy intestine had occurred, and the involvement had extended from the original site in the terminal part of the ileum to include almost five feet of the bowel immediately proximal to the original lesion. The patient had lost fifty pounds and was greatly disturbed by severe abdominal cramps and spells of nausea and vomiting and she was decidedly restricted in her activities because of evacuation of her bowels ten to fifteen times daily. It was evident that this patient's condition did not warrant further temporizing and her physician referred her to the clinic for surgical attention. Resection was carried out in one stage, removing all of the involved portion of ileum, the cecum, and ascending colon, with wide extirpation of the mesentery and large mesenteric nodes. The continuity of the bowel was re-established by ileotransverse anastomosis. A more difficult resection could not be imagined as the whole of the terminal segment of ileum and the cecum formed one large, beefy, phlegmonous mass, which was adherent in the right iliac fossa and had to be freed from such retroperitoneal structures as the ureter, ovarian vessels, and iliac vessels. The patient's postoperative course was uncomplicated except that there was some infection of her wound. One year later she reported a gain of thirty pounds, freedom from all discomfort, and a normal state in all respects except a tendency to have loose bowel movements (averaging about four stools daily).

It is difficult to understand how any physician could conscientiously advise such a patient to forego surgical intervention and to continue to



Other lesions to be considered are the specific granulomas, such as tuberculosis, syphilis, actinomyces, amebic or parasitic tumors; various types of malignancy, such as scirrhus carcinoma, lymphosarcoma or Hodgkin's disease, and mass-producing lesions of the female adnexa and cecal appendix. It is certain that the malignant processes and the mass-producing lesions cannot be ruled out definitely except by performing an exploratory operation.

If a fecal fistula is present, besides making an investigation for acid-fast bacilli and sulfur granules, one must take into consideration the possibility of a foreign body, appendiceal abscess, or sequelae of a surgical accident being present.

Finally, the diagnosis is achieved when clinical suspicion has been fortified by a suggestive roentgenographic deformity and the elimination of all other etiologic factors to such an extent that laparotomy is deemed justifiable. However, the diagnosis is accomplished with certainty only after the diseased portion of bowel has been resected and examined grossly and microscopically.

In one-fourth of the cases the condition had been diagnosed correctly prior to observation at the clinic. In the remainder of the cases the order of frequency of other diagnoses was as follows: appendicitis, chronic ulcerative colitis, amoebic dysentery, fecal fistula, tumor of the bowel, duodenal ulcer, pelvic tumor, tuberculosis of the cecum, intestinal obstruction, and irritable bowel. Sixty-seven different diagnoses were made in 35 of the cases; in 9 cases a diagnosis had not been made; 40 of the 44 cases were correctly diagnosed at the clinic before surgical intervention.

The presence of three cardinal features is of great aid in reaching a correct diagnosis. In our series a palpable mass was present in 31 cases, chronic obstruction of the small bowel occurred in 28, and positive signs were observed on roentgenologic examination in 36 out of 39 cases. The remaining 5 were not given either the barium meal or the enema as obstruction was nearly complete. Of the 44 cases, only 2 did not have any of these features; 21 exhibited all three features, and in 12 others only one of the three features was lacking. Of 9 cases in which only one feature was present, roentgenographic evidence of the disease was obtained in 6, obstruction was found in 2, and a palpable mass was detected in 1. It is evident that in 95 per cent of the cases some of the three features will be found in combination, and, if the history is suggestive, if the roentgenologic examination of the thorax does not reveal a tuberculous process, if fever of low grade is present and the sedimentation rate is elevated, the clinical diagnosis is assured as nearly as is possible before exploration.

#### TREATMENT

There is no known medical regimen of value in curing this malady. Spontaneous cures have been recorded by the majority of observers who

phase, a simple short-circuiting operation carries a very low mortality and provides an opportunity for the diseased segment of bowel to improve by being placed at rest. If the trouble continues to advance subsequently, resection can be undertaken with the advantage of having one stage of the operation completed and of having the organism adjusted to the unnatural fecal pathway.

For those among whom the pathologic process is so far advanced that temporizing has nothing to offer, primary radical extirpation of the diseased segment, if at all feasible, has much in its favor. This is particularly true if only the terminal portion of ileum is involved, or, at the most, the terminal part of the ileum and its adjacent colonic segment. In these instances, there is the choice of performing ileocolostomy with or without division of the ileum and of making a resection at that same time or at a subsequent time. In the advanced stage of the disease, such as was present in the majority of our cases, obstruction, fistula or both have developed and side-to-side ileocolostomy without transection of the ileum would only partially deviate the fecal current, and the cramping pain, reflex nausea and vomiting and even the diarrhea would not be completely relieved. With this situation obtaining, the patient can make very little headway in preparation for the second stage of the operation. Furthermore one is frequently disappointed if it is expected that with the involved segment only partially at rest the infection will subside and will permit resection to be made more easily. If ileocolostomy alone is to be employed, it is true that the fecal current can be side-tracked completely by transecting the ileum proximal to the diseased region and by inverting the distal stump. However, if the obstruction is severe an almost "blind segment" obtains and there is the possibility that a blowout of the closed stump will occur. Also, reflex disturbances and toxic manifestations continue unabated in some of the cases. Extension of the disease has been known to occur between the two stages of the operation with ensuing involvement of the region of anastomosis. Should the disease extend after ileocolostomy, which has been accompanied by transection of the ileum in an uninvolved proximal segment, it would seem highly probable that the spread occurred by way of the diseased mesentery and lymphatic structures which were left in situ.

When ileocolostomy is made to prevent the flow of feces through a fistulous tract, it is evident that the entire fecal current must be side-tracked. Even then, although the feces no longer extrude through the abnormal opening, the origin of the tract in the infected segment of intestine has not been disturbed and will not close. Occasionally, when a large quantity of fluid and unabsorbed elements of food are being lost through an external fistula and there is severe excoriation of the abdominal skin, it would seem logical to precede resection by diversion of the intestinal contents as described. Thus rehabilitation in this way undoubtedly would make the risk of resection less. However, it is unusual

adhere to a regimen that, if carried further, would certainly have had a disastrous result. Anyone who has observed a case such as that described or who has seen the irremediable damage sustained by the affected segment of intestine must realize that there is no known medical treatment that will dissolve the fibrotic stenosis which has replaced the normal elements or that will close the fistula that develops in the later phases of terminal ileitis. However, it is conceivable that a specific remedy may be found eventually that will allay the disease in its early stages or will prevent recurrence of the process after surgical removal of the damaged or fistulous bowel.

Twenty-seven patients had undergone some operation before coming to the Mayo Clinic. These procedures consisted of 24 appendectomies, 6 ileocolostomies, and 4 resections. Exploration or drainage of an abscess brought the total to 41 operative procedures. Sixty-two operations have been performed at the clinic on this same group of patients, bringing the total number of surgical interventions for the 44 individuals to 103.

After surgical intervention has been decided on, much further thought and consideration will be required to determine the exact procedure most suited to the case (Table VI). Should one attempt resection and anasto-

TABLE VI  
REGIONAL ENTERITIS: DETAILS OF SURGICAL TREATMENT IN 44 CASES

SURGICAL TECHNIQUE EMPLOYED		INDIVIDUAL FREQUENCIES	SUBTOTALS
Ileocolostomy*	End-to-side	1	14
	Side-to-side. Cut across in 3 cases, not cut across in 10	13	
One-stage resection†	Ileocolostomy and resection of transverse colon, side-to-side	12	14
	Ileocolostomy and resection of ascending colon, end-to-side	1	
	Exteriorization	1	
Two stage resection	Ileocolostomy with transverse colon, side-to-side	12	15
	Ileocolostomy with ascending colon, end-to-side	2	
	Ileo-ileostomy, side-to-side	1	
Exploration	With freeing of adhesions	1	1

\*One ileostomy performed.

†Witzel enterostomy also performed at the time of resection in 8 cases.

mosis in one stage, which will save the patient time and expense, or would it be more judicious to approach the problem conservatively by making a simple ileocolostomy as a primary procedure, carrying out a resection only after a period of observation? Curiously, experience has led to the practice of employing the more radical procedure in those cases in which the pathologic process is most advanced and in which, from a theoretic standpoint, the operation is not likely to be tolerated well. The logic of this is readily discernible when one recalls that in the early stages of the disease the process has been known to subside spontaneously. In this

which embolism, intestinal obstruction, and hemorrhage occurred, death ensued. Severe debility associated with a state of deficiency and pneumonia was responsible for one additional death.

One to two years after surgical treatment, 4 patients were dead, 5 were in good health, 2 were either unimproved or were in a worse condition than before operation, and 3 reported a gain in weight but the latter had been operated on too recently to foretell their ultimate course (Table VII).

TABLE VII  
REGIONAL ENTERITIS: RESULTS OF SURGICAL TREATMENT IN 44 CASES  
(6 Mo. to 2 Yr. POSTOPERATIVELY)

STATUS	OPERATION			
	ILEOCOLOSTOMY	ONE-STAGE RESECTION	TWO-STAGE RESECTION	EXPLORATION
Dead	4	1	2	
Good	5	12	12	
Poor	2			
With persistent fistula	3			
Unchanged		1	1	
Not reported				1
Total	14	14	15	1

In several of the cases in which resection in two stages was performed, ileocolostomy had been carried out primarily, but continuation of the symptoms or progress of the disease was responsible for the decision to employ resection. The average time between stages was three months, although in one case resection was carried out within two weeks of the time of ileocolostomy and in another, one year lapsed before the second operation. The type and situation of the anastomosis in the 15 cases is of interest: In 12 instances ileotransverse colostomy was performed and in 2 the ileum was attached to the ascending colon. Twelve of the 14 ileocolostomies were made by lateral anastomosis and 2 were effected by end-to-side union. The ileum was transected and the distal stump inverted in 3 of these cases. In the remaining case, the midileum was involved and side-to-side ileoileostomy was performed and was followed six months later by removal of the segment. The terminal portion of ileum, cecum, ascending colon, and a part of the transverse colon were removed in 10 cases; in 3 the resection embraced the terminal portion of ileum, cecum, and first portion of the ascending colon; in 2, a large segment of the involved midileum alone was extirpated. One patient was subjected to another anastomosis between the ileum and sigmoid two years after the original resection was performed because of a recurrence at the site of the anastomosis and in the transverse colon. The patient died and this was the only surgical death in the group. His death followed development of a fecal fistula, infection of the wound, and general sepsis.

for the fistula accompanying regional enteritis to be that extensive; the debility which is present is generally that occasioned by the presence of the disease rather than by loss of the substances mentioned. For this reason very little is attained by a simple short-circuiting procedure. In the 9 cases of fecal fistula, 18 operations had been performed before the patients came to the clinic and regardless of these procedures the fistula had not been eliminated. The fact is that in each instance the fistula occurred after performance of an operation at which time the diseased bowel was not removed.

What may one expect from resection and anastomosis in one stage when the disease already has progressed to a late phase? It will be found that the patient obtains relief from his discomfort, that extensive progress of the disease toward an uninvolved region is obviated as nearly as possible, that fecal fistulas are eliminated if present, and that the likelihood of occurrence of a fistula postoperatively is extremely remote. Also, the return of the patient to his normal pursuits has been expedited by many months. The only question then is: Does an operation in one stage subject the patient to an unjustifiable and avoidable risk? Observations do not warrant such a conclusion if one considers the results obtained in properly selected cases. Most of the patients who had regional enteritis were in the period of life in which surgical intervention is withstood particularly well. Also, the attending circumstances seem to militate against the likelihood of the occurrence of that most dreaded and very frequent complication of intestinal surgery; that is, peritonitis. The infection in the wall of the intestine has exposed the peritoneal cavity to contamination for such a lengthy period in most cases that considerable immunity to subsequent infection has apparently ensued. Peritonitis was not the cause of death in any case in our series.

Among older patients, in the upper limits for the occurrence of such a process, and particularly among those who have involvement in several regions of the small intestine, the conservative procedure would seem to be a necessity. This is especially true if an abscess has formed. The surgical procedures undertaken on behalf of the patients in our series consisted of 14 side-tracking operations (13 ileocolostomies and 1 ileostomy); 15 resections in two stages, 14 resections in one stage, and 1 exploration with the freeing of adhesions (Table VI).

Of 14 exclusion procedures (ileocolostomies), 13 were effected by side-to-side anastomosis (12 to the transverse colon and 1 to the descending colon); in 1 case the intestines were anastomosed end-to-side. In 3 instances the ileum was divided and the distal stump was inverted. The ileostomy was of the loop type, with both the distal and proximal stomas exteriorized. The postoperative complications in these cases were acute diarrhea, 2 patients; fecal fistula, 1; infected wound, 2; otitis, 1; intestinal obstruction, 1; hemorrhage, 1; and embolism, 1. In the cases in

sitating subsequently a total exclusion operation, after which the patient died of obstruction. The fourth death was that of a boy for whom ileostomy had been performed. An inadequate resection had been carried out elsewhere (apparently a short segment of ileum had been removed and the remaining ileum had been anastomosed with the cecum which was very likely diseased). Furthermore, the involved mesentery and regional lymph nodes were only partially removed in order that the cecum and ascending colon might remain in situ. Recurrent symptoms of a fulminating character soon made themselves manifest and, when this patient came to the clinic less than a year after the resection, involvement had extended distal to the original site as far as the sigmoid flexure. Fifteen days postoperatively, death ensued from a combination of conditions: deficiency, anemia, toxemia, hemorrhage, and pyoderma gangrenosum.

Two patients died after anastomosis and resection were performed in two stages. Both had had inadequate treatment although according to the history the disease was extensive at least two years before they came to the clinic. One of these cases was that of a man, aged 30 years. After the inadequate resection, he was fairly well for one and one-half years. Recurrence or continuation of the disease resulted in involvement of the distal portion of ileum and of the ascending, transverse, and descending colon with perforation and with formation of an abscess. Ileosigmoidostomy was performed but the patient died thirty-six days postoperatively. The other death occurred nine months postoperatively and has been described previously. In this case, also, the colon was extensively involved.

The single death, three months after the one-stage procedure was carried out, apparently would have occurred regardless of the type of treatment employed. All of these deaths, except one, occurred among patients who were at either one or the other of the extremes of the age group for the disease; that is, they were either in their teens or were more than 50 years of age. It would seem that both the old and the young who have regional enteritis are particularly susceptible to the disease or are less prone to develop resistance and immunity to its progress than are those of middle age. It will be found also that three of the deaths occurred after recurrence or extension of the inflammatory process had taken place with involvement of a large part of the colon. If such an eventuality transpires, the outlook is always extremely grave and surgical intervention has been fruitless.

A résumé of the results from all types of surgical treatment shows that improvement occurred in 33 cases (including 1 in which exploration alone was performed), that improvement did not occur in 4 cases, that 5 surgical deaths took place, and that 1 death ensued three months postoperatively and another nine months postoperatively. Three of the deaths were definitely attributable to extension of the disease. The opera-

The other postoperative complications among this group of patients were: pneumonia in 2, epididymitis in 1, gastric retention in 3, fecal fistula in 2 (closed spontaneously), and pharyngitis in 1.

What were the results of the two-stage procedure? There were 2 deaths, the one aforementioned and one nine months postoperatively (Table VII). In the latter instance, even at the time of the resection, the process had extended to the transverse colon. Diarrhea had increased in severity and there was an ensuing deficiency syndrome simulating pellagra. Finally, pneumonia was superimposed and death occurred. One of the 13 patients reported being in the same condition as before operation; 12 were well and had gained on the average about fifteen pounds. However, less than six months had lapsed since completion of the surgical treatment of 4 of the latter group and the ultimate results are not yet certain.

Resection in one stage was performed with 13 anastomoses of the ileum to the transverse colon or to the hepatic flexure. Simple exteriorization of the terminal portion of ileum and ascending colon, as a modified Mikulicz procedure, was effected in 1 instance. A side-to-side anastomosis was used in all except 1 case in which end-to-side union was made. A Witzel type of catheter enterostomy was provided proximal to the anastomosis in 8 instances.

There were no surgical deaths among patients who had a resection in one stage (Table VII). The complications encountered included abscess in one case, infected wound in 3, ileus in 2, gastric retention in 1, acute dilatation of the stomach in 1, embolism in 1, and pneumonia in 1.

The results of such treatment were as follows: One patient died four months postoperatively from multiple thrombosis of doubtful association with the disease under consideration. Twelve patients reported good results including an increase in weight from ten to thirty pounds. One patient's condition was seemingly unchanged: the diarrhea persisted and a seclusion type of personality had developed. However, 4 of the patients who stated that they had made good progress mentioned having three to six loose bowel movements daily. The length of time since surgical interference was more than one year in 9 instances; it was less than that in the remaining 5 cases of the group.

A study of the causes of death furnishes some very interesting information concerning the selection of operation. Four of the patients died after performance of a short-circuiting operation; in 3 of these cases the procedure was performed as the first stage of a two-stage operation; in the fourth case ileostomy was provided in an attempt to place a completely involved colon and ileum at rest and was intended only as a palliative measure. The 3 patients having ileocolostomy died from embolism, hemorrhage from the ulcerated portion of ileum left in situ, and failure to transect the ileum in which a fecal fistula was present, neces-

consideration of postoperative care, emphasis has been placed on the necessity of directing attention toward the correction of nutritional deficiency and to keeping the intestine decompressed. The use of a high concentration of oxygen in the inspired air has been found efficacious for this latter purpose.

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tive mortality rate based on the total number of cases was 11.5 per cent, but, if calculated on the basis of the number of operations, it was 8 per cent.

Postoperative care undoubtedly has much to offer toward decreasing mortality and morbidity among these extremely ill patients. Besides the usual symptomatic care accorded patients after operation, there are two phases of the condition of patients who have regional enteritis that are particularly worthy of consideration. First, severe deficiency in nutritional elements has occurred as a result of the inroads of the disease and for several days after operation nothing can be taken by mouth to replenish these deficient stores. The judicious use of crystalline vitamins in solutions intravenously, restoration of basic elements by intravenous administration of sodium chloride and calcium chloride, replacement of serum proteins and of hemoglobin by transfusions of blood, all have a place in properly selected cases. Secondly, measures for decompression of a diseased bowel or, better still, the prevention of distention, retention, and ileus have a prominent place in postoperative therapy. Transduodenal continuous aspiration (Paine and Wangenstein<sup>31</sup>) is instituted at the earliest sign of such an occurrence. A rectal tube is inserted at regular intervals to prevent excessive accumulation of colonic pressure. In the majority of the cases in which we have employed resection in one stage, a Witzel type of enterostomy made proximal to the anastomosis has been provided at the time of the radical procedure. Gentle suction (about 30 cm. siphonage pressure) is applied to the catheter in the same manner as to the Wangenstein duodenal tube. This in itself is usually sufficient to keep the bowel decompressed. Recently, the Boothby,<sup>32</sup> Lovelace,<sup>33</sup> Bulbulian<sup>34</sup> oxygen apparatus has provided a very valuable addition to our armamentarium. The value and mechanism of an intake of a high percentage of oxygen in decompression of the bowel was noted by Fine, Sears, and Banks<sup>35</sup> in 1935. With the development of an efficient, convenient, and cheap apparatus for administration of 90 to 95 per cent oxygen, the procedure is feasible clinically and is highly efficacious therapeutically.

#### SUMMARY

The subject of regional enteritis has been considered from a general historical standpoint. Specific data obtained from the study of forty-four proved cases of regional enteritis have been presented. A conjecture as to the role of a filtrable virus as a causative agent has been advanced. The occurrence of three cardinal features, that is, a mass in the right lower quadrant of the abdomen, the presence of chronic intestinal obstruction, and positive roentgenographic details, has been shown to be present either singly or in combination in 95 per cent of the cases reported in this series. Surgical procedures have been discussed in detail, also their probable relationship to recurrence and to fatalities. In the

# Review of Recent Meetings

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## REPORT OF THE ELEVENTH MEETING OF THE INTERNATIONAL SURGICAL CONGRESS, BRUSSELS, BELGIUM, SEPT. 18-22, 1938

ALBERT O. SINGLETON, M.D., GALVESTON, TEX.

**H**ISTORICAL Belgium is the logical place for an international meeting. Just outside of Brussels is the field of Waterloo, and there are many reminders of the recent world struggle on every hand. The International Surgical Society began its eleventh meeting in the beautiful Senate Chamber of the Palace of the Nation where some fifty patriots were condemned to death by the enemy for being loyal to their country, among them Edith Cavell.

In spite of an international crisis hovering over Europe, for five days all reference to national and racial differences was laid aside, and surgeons of all nations, friendly or hostile, gave a united interest to many important surgical problems. It is not inappropriate to mention that the presiding officer of the Congress was America's own beloved Professor Rudolph Matas of New Orleans. With a world-wide reputation as a scientist, a courtly manner, and a mastery of many languages, he seemed to be made for the honored position. He addressed the meetings in French, with frequent side remarks to distinguished Fellows from Spain, South America, Italy, or Germany in their own tongue. International members, as well as Americans, paid homage to this great and learned American surgeon.

The scientific sessions were held at the Auditorium of the Faculty of Medicine, while operative clinics were held at Hospital Saint-Pierre and Hospital Brugmann in Brussels and at the Surgical Clinics of Louvain.

A symposium on the Surgical Treatment of Hypertension was the subject for the first day, and the following papers were presented:

**M. N. Pende, Rome: Introduction to the Problem of the Surgical Cure of Arterial Hypertension.**—The surgical treatment of essential hypertension was proposed by him for the first time in 1924 with the resection of the greater and lesser left splanchnic nerves. The operation was performed for the first time in Italy by Pieri, of Udine, in 1929 and by Durante, of Genoa, in 1930 with favorable results.

The experimental and clinic basis of the operation proposed by him in the treatment of arterial hypertension is due to some extent to the knowledge (to which he has contributed since 1903) of the action that the resection of the splanchnic nerve has in reducing the adrenalin secretion of the corresponding suprarenal gland; to some extent on the extensive vasodilator effect that even the resection of the greater and the lesser left splanchnic nerves only has on the abdominal vessels; to some extent finally on the probability that the resection of the splanchnic nerve abolishes hypertensive reflexes, especially in the vascular abdominal field.

The operation introduced by Pende must be strictly limited to the hypertension cases, especially in young adults before senility in whom careful clinic examina-

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sympathetic chain. Excision and division must be rejected because they are also useless. Simultaneous excision of the chain may be indicated when a lesion has been located upon it.

**M. M. Peir and Alfred E. Smith: By Invitation: Surgical Treatment of Hypertension.**—Hypertension is a symptom of some constitutional disease; manifestly, itself is excessive activity of the sympathetic nervous system, probably due to some lesion from the adrenal or the kidney. We can symptomatically relieve it by denervating the abdominal viscera. This denervation can be accomplished easiest and safest by an approach to the sympathetic chain; i.e., the splanchnic, major and minor at the level of the eleventh rib, extrapleurally at the sites of the holes of the vertebrae. Dr. Peir demonstrated this approach. The operation has the advantage of being less severe than others, making it possible for both sides to be denervated at the same time. He reported more than 300 patients operated upon, many with remarkably good results, others with indifferent results and some failures. After this experience he felt that the operation was justified in a great many patients and gave indications for the operation. He proposed to continue this procedure as long as it proved as useful as it apparently had during the past several years. This paper was well received by the Congress.

The foregoing papers were discussed by: M. M. C. Heymans, Ghent; A. Chlasiński, Poznań; E. dos Santos, Lisbon; A. Dickson-Wright, London; P. Cokkalis, Athens; E. Cullen, Boston, Mass.; C. Jeanneret, Bordeaux; J. Arce, Buenos Aires; W. Walters, Rochester, Minn.; A. Valerio, Rio de Janeiro; M. Donati, Milan; E. Fontaine, Strasbourg; Boghos Bied Ghali, Cairo; A. Jirasek, Praha; R. Appelmann, Louvain; M. Boglietti, Modena; J. Bedna, Hradec Králové; A. Jentzen, Geneva; S. Ceruga, Cairo; S. de Dzierbowski, Bydgoszcz; E. Derom, Ghent; J. Strombeck, Stockholm; J. Jancu, Bucharest; J. Govaerts, Brussels; J. C. dos Santos, Lisbon; M. Hilarowicz, Lwów; M. Michon, Paris.

The discussions embraced various phases of the question, some predicting further success with surgery, and others stating the opinion that the present surgical practices would be abandoned as of no benefit for hypertension. Other papers, of shorter duration, which were not on the official program, were read. The titles are as follows: Dr. Ramon Palacio Pease, Buenos Aires: New Surgical Treatment of Mammary Ptosis; Dr. Bernard, Giessen: Anastomosis Between the Gall Bladder and the Intestinal Tract; Dr. H. Paschaud, Lausanne: Action of the Electromagnetic Waves in Operative Surgery; Dr. C. Daniel and Dr. Mavrodin, Bucharest: Treatment of Hypertension by Block Anesthesia; Dr. Klapp and Dr. Baumann, Göttingen: The Position of the Wire Extension in Repairing Fractures (slides); Dr. Reschke, Griefswald: The Manner of Handling Bleeding Tumors of the Stomach; Dr. Lexius, Heidelberg: The Artificial Blood Supply of the Kidney; Dr. Jaeger, Munich: The Method for Stomach Operations; Dr. Schorcher, Munich: A New Apparatus for Intravenous Blood Transfusion; Dr. A. Lob, Munich: Procedure in Stomach Operations; Dr. R. Gebhardt, Hohenlychen-Mark: Hohenlychener Film; Dr. L. Seiffert, Neunkirchen: Is It Possible to Totally Remove the Bladder Nowadays, and What Are the Conditions for a Successful Plastic Replacement of the Bladder?

**Symposium on Bone Grafts:** M. B. Cunco, Paris: Introducing the Question of Bone Grafts.—The method of bone grafting that gives the best results now is the autoplasmic one, which can be used in various ways, the choice of which depends on the local conditions under which it will be used. The superiority of an autoplasmic graft is of an hormonal nature, but the success of a graft depends essentially on the condition of the receiving bone. Osteoplastic grafts which possess

expectedly. Frequently, when it is a primary occurrence, it is related to some renal disorder.

The authors then proceed to discuss the methods of differential diagnosis of paroxysmal hypertension, arteriosclerosis, renal sclerosis, and, in particular, the tests establishing the stage of the organic lesions and the importance of the functional disturbance.

Operative treatment is indicated when the organic changes are slight or lacking altogether, when medical treatment is of no avail, and when the disease is not secondary to a renal sclerosis. Surgical treatment in favorable cases may arrest the disease; in the majority of cases it can bring about a clinical recovery in patients by dispelling their subjective troubles, and in a smaller percentage of cases it may restore to normal level or may considerably reduce the increased blood pressure.

The results of surgical treatment available at present should induce practitioners of internal medicine to collaborate more actively with surgeons. Such a collaboration is desirable not only in the interests of the patient, but also because the investigation of clinical cases thus will become more complete; diagnosis, more exact; and the choice of subjects to operate upon, much easier. In short, judging from the results of surgical treatment, we can say that, with all the methods used and enumerated, a few favorable results have been obtained. That, in itself, is sufficient reason for surgeons to continue research and experiments, the more so as the good results obtained at present cannot be achieved by any other means. All surgeons seem agreed that the best results are obtained in essential juvenile forms, uncomplicated by arteriosclerosis or renal sclerosis; associations with diabetes, obesity, and menopausal disturbances do not appear to be of any importance. The application of the various operative methods is still in the experimental stage and, therefore, still dependent on personal choice rather than on any indication based on broad and definite comparative experience.

Sympathetic surgery is indicated only in cases free from vascular sclerosis, even though they are associated with diabetes, localized cerebral symptoms, and symptoms due to intracranial tumors, in which case it is sometimes necessary to carry out decompression trepanning. Selecting patients likely to benefit by operation is today a duty incumbent on the surgeon. Although there are several procedures, the authors give preference to alcoholization of the splanchnic. Alcoholization of the splanchnic may be indicated also in cases of sudden rise in tension, where it is necessary to lower the pressure rapidly. If there is a favorable result, it is made permanent by operation on the sympathetic. Splanchnic interruption is the fundamental stage of all the proposed modifications, but none of the modifications of Pende's operation present any real advantage for they are mere complications of a simple procedure without any sequel. Lumbar ganglionectomy is useless and injurious; resection of the anterior roots according to Alessandri and Valdoni, must be definitely rejected because of the heavy burden of abdominal muscular paralysis and the severity of the operation. In unilateral resection of the greater and lesser splanchnics, exploration of the suprarenal may be done, for it shows up the possible presence of a hyperplasia or tumor. At the same time, direct exploration of the kidney will permit of a more exact diagnosis of its pathologic condition. If, after such intervention, no good or adequate result is achieved, a second stage may be undertaken consisting of right splanchnic resection with total adrenalectomy.

Single stage operations on the adrenals are indicated in cases where one is led, by the presence of hypertensive crises, to suspect a suprarenal tumor or hyperplasia. What is important, especially in hyperplastic cases, is the presence of

suprarenal excess. Enervation and resection must be rejected because they are also valueless. Simultaneous exploration of the adrenals may be indicated when adrenalectomy has been decided upon.

M. M. Peet, Ann Arbor, Mich. (by invitation): **Surgical Treatment of Hypertension.**—Hypertension is a symptom of some constitutional disease manifesting itself in excessive activity of the sympathetic nervous system, probably due to some hormone from the adrenal or the kidney. We can symptomatically relieve it by denervating the abdominal viscera. This denervation can be accomplished easiest and safest by an approach to the sympathetic chains; i.e., the splanchnic, major and minor, at the level of the eleventh rib, extrapleurally at the sites of the bodies of the vertebrae. Dr. Peet demonstrated this approach. The operation has the advantage of being less severe than others, making it possible for both sides to be denervated at the same time. He reported more than 300 patients operated upon, many with remarkably good results, others with indifferent results and some failures. After this experience he felt that the operation was justified in a great many patients and gave indications for the operation. He proposed to continue this procedure as long as it proved as useful as it apparently had during the past several years. This paper was well received by the Congress.

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**Symposium on Bone Grafts:** M. B. Cuneo, Paris: **Introducing the Question of Bone Grafts.**—The method of bone grafting that gives the best results now is the autoplasmic one, which can be used in various ways, the choice of which depends on the local conditions under which it will be used. The superiority of an autoplasmic graft is of an hormonal nature, but the success of a graft depends essentially on the condition of the receiving bone. Osteoplastic grafts which possess

this hormonal power of stimulating bone formation on the surface of the receiving bone cannot exert their power unless the receptor is viable and shows the special activity itself. Autoplastic grafts are by far superior to homoplastic ones and still more so than heteroplastic material. It is better to use Orell's os purum than any nonautoplastic graft, but at the moment it is not possible to state definitely what is the osteogenic property of this os purum, save that it possesses it in a much less degree than does autoplastic material. It would perhaps be interesting to investigate the possibility of conferring an artificial osteogenic power on os purum.

The os novum formed by the tissues of the patient on whom the graft is proposed to be used can really be considered as an autoplastic graft of young bone. It seems to be an extremely interesting material, though its complicated technique must be borne in mind.

The age of the patient at operation is of prime importance, and the best results are obtained in children. There is a good chance of success in adults in good general health, as were the wounded of the last war. One must be much more reserved in considering patients who are more than fifty years of age.

**M. Fr. Albert, Liege: Biological Study of Bone Grafts.**—A collation of the vast literature and experimental work carried out in his laboratory has led Albert to the following conclusions:

Bone grafting is essentially a biological phenomenon, in which the essential role is played by the cells hereditarily adapted to bone formation. The superficial cells alone are capable of surviving and being grafted. The greater part of a bone graft is reabsorbed and replaced by new bone. For this replacement to take effect, however, the graft itself must furnish its own osteogenic cells, or else get them from the host on the spot (osseous stumps, site of fracture, or periosteum). Consequently, the living autogenous bone graft, partly covered over by periosteum, is always the ideal material. It alone can insure the success of a graft, when there is gross loss of osseous substance. The technique employed therefore should preserve to the full the unimpaired condition of the transplant cells and the vitality of the receptor tissues.

Dead bone may give favorable results, provided it has no antagonistic effects on the host tissues and can obtain from the host the osteogenic cells it lacks itself. The most practical type of dead bone is Orell's os purum.

For serious loss of bone substance or large interosseous space, os purum is an insufficient guarantee of success. In such cases, Orell himself has suggested the use of os novum, which he obtains by introducing dead bone chips under tibial periosteum. In this way the subperiosteal cells, which are intensely osteogenic, rapidly multiply, so that the young tissue invades the whole dead bone. Os novum is biologically equivalent to a living autoplastic graft and demonstrates in masterly fashion the very important role of the living osteogenic cell in rehabilitating and replacing the transplanted graft by new bone.

**M. D. B. Phemister, Chicago: Bone Transplantation in the Treatment of Tumors and Dystrophies of Bones.**—Relatively few bone sarcomas treated by resection and bone transplantation have been reported in the literature and in such cases local recurrence has been the rule. Tardiness in diagnosis is the chief obstacle to success. Five cases are reported. Two had local recurrences and metastases and died. Three were well  $2\frac{1}{3}$ ,  $4\frac{1}{2}$ , and 7 years after operation. Benign tumors and bone cysts may usually be treated successfully by simpler methods not involving the use of the bone transplant. Advanced or complicated cases of benign giant cell tumor, solitary bone cyst, regional osteodystrophia fibrosa, Paget's disease, and fibroma of mandible calling for bone transplantation are recorded.

M. Bahld, Wurzburg (replacing Prof. M. Kappis, who died several weeks before the meeting): **Bone Transplants in Chronic Infections and Diseases of the Limbs.**—The value of bone grafting in chronic inflammatory conditions of the joints appears (1) in the formation of arthrodesis, (2) in rebuilding the rim of a joint cavity, and (3) in serving certain "biological ends."

Arthrodesis according to the methods of Albee and Hibbs, or other methods, is used in extremely varied conditions of the vertebral column. Five hundred cases are quoted from the literature of instances where sacroiliac arthrodesis was effected by the transplantation of pieces of bone; in this series 90 per cent of patients were either cured or greatly relieved. In the case of the hip, the transplantation of bone finds a use in arthrodesis, in building up a posterior buttress for the acetabulum, or in bone-pegging around the joint; the question of drilling the neck of the femur deserves investigation.

Bahld closed his paper with a discussion of the aims and methods of bone grafts considered in relation to the joints of the knee, the foot, the shoulder, the elbow, and the hand.

M. Sv. Orell, Stockholm: **Bone Grafts in the Treatment of Tuberculous Osteitis and Arthritis.**—The author reviewed the general literature on the use of bony grafts in the treatment of bone and joint tuberculosis after the extirpation of the focus and resection of the bones and joints and in arthrodesis, particularly in spondylitis and tuberculous coxitis. The problem is surveyed in the light of the studies the author has previously conducted on the formation of new bone in experimental and clinical bone grafting which resulted in the introduction of two new forms of bone graft, called *os purum* and *os novum*. The former is dead bone which has been chemically and physically freed from fat, connective tissue, and protein; the latter is living, newly formed, soft, pliable bone which after subperiosteal implantation of *os purum* on the tibia has been obtained as a periosteal coating which after transplantation can more easily take up nutrition than can fresh live bone. The surgeon can thus perform bone grafting as previously with fresh autoplasmic bone, compact or spongy, freely transplanted or pedunculated, or he can use *os purum* or *os novum*. Compact and spongy *os purum* can be stored up in the dry condition and sterilized immediately before using by boiling in physiologic NaCl solution. The different types of bony graft can be employed alone or in combination. It is advantageous to place a compact graft against compact bone and a spongy graft in order to obtain the best possible bony union. The surgeon is thus able to vary and combine the grafting material considerably, depending on the nature of each individual case, the location of the tuberculous focus, and the structure of the bed of the new graft.

With general hygienic dietetic therapy as the basis of the treatment, it is often possible to shorten the course of the cure after removal or healing of the tuberculous osteitis by doing a bone transplantation to secure new formation of bone or bony union, so that complete restitution or a firm bony union is obtained within the tuberculous region. The danger of recurrence especially after arthrodesis cannot be entirely eliminated, but the recurrence apparently can be better controlled than when these operations are not done.

Whether the transplanted bone has any influence on the tuberculous process itself is extremely difficult to decide definitely. It is obvious that the bone graft stimulates the tissues around to formation of new bone which goes on actively in the soft tissues in the bone canaliculi and on the surface of the bone. In this way the graft can speed up and ensure bone healing of the tuberculous focus. It also seems probable that the bony graft has a more general influence on the organism.



M. R. Demel, Wien, spoke on *Indications for a Free Introduction of a Piece of Bone in New Fractures and Pseudarthrosis*.

Harry Platt, Manchester: *Bone Grafting in Recent Fractures and Pseudarthrosis*.—(1) in recent fractures bone grafting is an ineffective method of securing internal fixation when compared with other forms of osteosynthesis such as plating. (2) The essential distinction between delayed union and true non-union must be recognized. (3) Delayed union is a temporary suspension of osteogenesis which, in the majority of cases, can be successfully treated by conservative methods. Premature operative interference is to be condemned. In certain circumstances union may be hastened by drilling the fragments at the site of the fracture. Additional osteogenetic stimulus may be provided by a limited type of bone graft in the form of an osteoperiosteal, sliding, spongiosa, or peg graft. (4) In true nonunion a bone graft is required to act as a mechanical strut, as a conductor of bone, and as a producer of bone. The tibial graft best fulfills these requirements in pseudarthrosis of the long bones. (5) Two standard methods of insertion of the bone graft are of established value: (a) the inlay and (b) the onlay or massive graft. (6) In the compound injuries of civil life the two-stage operation used in the treatment of gunshot fractures is rarely necessary. (7) Failures after bone grafting are usually the result of technical faults, most of which are avoidable. The main causes of fracture are (a) infection, (b) inadequate contact between graft and host bone, and (c) insufficient immobilization. In a graft used to bridge a long gap, absorption or spontaneous fracture may occur in spite of an efficient technique. (8) The least favorable sites for successful grafting are the shaft of the femur, lower third of the tibia, and lower third of the humerus.

Papers on bone grafts were discussed by the following:

Mm. R. Alessandri, Rome; O. Haberland, Cologne; Fr. de Quervain, Berne; R. Danis and F. Jonckheere, Brussels; J. de Fourmestaux, Chartres; D. Ferey, Saint-Malo; M. Zahradnick, Praha; L. and F. Berard, Lyons; A. Lambotte, Antwerp; R. Fontaine, Strasbourg; R. Zanolì, Pietraligure; Fr. Cleret, Chambéry; Gonzalez-Aguilar, Barcelona.

Symposium on the Surgical Treatment of Cysts and Tumors of the Lung: M. F. Sauerbruch, Berlin, gave the introduction.

M. H. Constantini, Algiers: *Physiological Conditions of Pulmonary Surgery*.—Increased knowledge of the physiopathology of the pleuropulmonary system acquired during recent years has altered our methods and made possible new operations on the lung. Pneumothorax is generally tolerated well by vigorous and healthy young subjects. It is the shock of the collapse which calls out the vaso-sympathetic reflex capable of arresting the heart beat. The pulmonary elasticity, by allowing a sudden contraction, is responsible for these reflexes. Pressure anesthesia, today made possible thanks to the nitrous oxide apparatus and intratracheal anesthesia, counteracts the sudden collapse of the lung. Atropine, by paralyzing the vagus, and ephedrine, by stimulating the sympathetic, also mitigate the effects of collapse. The exposed lung easily chills and the patient therefore must be constantly warmed during operation. Bronchial effusions may be abundant and may obstruct the bronchial tubes, even to the point of asphyxia. The cough reflex, which evacuates them, therefore must be carefully maintained. The patient is operated on in the inclined position for the same reasons. Ligation of the hilar bronchus does not generally have any immediately serious consequences. Postoperative pneumothorax will eliminate sudden collapse reflexes, while oxygen therapy will eliminate asphyxia.

Pulmonary atelectasis, the usual cause of which is obliteration of the greater bronchi by thick mucus, may necessitate surgical intervention to free these bronchi. After pneumonectomy, the subject will be easily fatigued.

Exploratory thoracotomy, today without danger, may be of the greatest service in making possible an accurate diagnosis and the carrying through of that treatment which seems most suitable.

**M. J. Arce, Buenos Aires: Surgical Treatment of Cysts and Tumors of the Lung.**—The author states that the treatment of pulmonary cysts and tumors is essentially surgical. His report is divided into five sections. The first part deals with the preparation of the patient for operation. The second is concerned with what he calls the pleural risk; that is to say, the technical difficulties arising from artificial pneumothorax. He deals in a detailed manner with the methods and procedures for avoiding these difficulties. He pleads for preliminary pneumothorax, but also describes the indications for pressure anesthesia, artificial formation of adhesions, and surgical pneumothorax (Bazy, Delageniere, Duval). The author favors early exploratory thoracotomy and total pneumonectomy in tumors of the lung.

**M. G. Forni, Venice: Methods and Results of Operations for Pulmonary Tumors.**—Pulmonary tumors are generally bronchiogenic carcinomas; sarcomas and benign tumors are rare. Only 10 per cent of these tumors admit of radical treatment; i.e., pneumonectomy and lobectomy. Tumors of the greater bronchi and their main branches may be removed by total excision of the lung in one stage by the anterior route. Circumscribed peripheral tumors of bronchiolar origin are amenable to lobectomy by various techniques, either in two stages in a freed pleura preceded by pneumothorax and phrenic evulsion, or in two or more stages when spontaneous or artificial adhesions are present. Results of operation culled from collected operative statistics consist of 33 total pneumonectomies, 62 lobectomies, and 92 atypical operations. Of the 33 pneumonectomies performed, 30 were one-stage operations for carcinoma; 3 were in two stages for sarcoma. There were 10 recoveries, 3 lasting several years; the others, from a few months to 1 year; 3 deaths from recurrence and 20 postoperative deaths. Lobectomies (62) were performed 58 times for cancer (57 primary and 1 metastatic) and 4 for sarcoma (2 primary and 2 metastatic); 38 lobectomies were done in one stage, and of these 14 were successful, some of them for several years' duration. Eleven had fatal recurrences and 13 died after operation. Of 24 lobectomies in two or more stages, 9 recovered, 5 had recurrences, and 10 died at operation. The atypical operations were found to be inadequate and incomplete and revealed the highest mortality.

**M. G. Baggio, Pisa: Methods and Results of Operations for Pulmonary Cysts.**—Pulmonary cysts are either autochthonous or parasitic (echinococcal) in type. Lack of observations and the endemicity make it essential, in studying the results, to supplement the numerical with a critical element. Autochthonous cysts differ surgically from echinococcal cysts. Hydatid cysts may be cured spontaneously by emptying themselves into the bronchi, but this is a contingency one no longer waits for, and it has been replaced by suitable methods of surgical treatment. It is shown how dangerous it is to operate on a free pleura, because of certain influences, both direct and indirect, on the freely exposed pleura, influences which are not manifest in cases where the pleura is excluded. If the operation on the free pleura sometimes gives brilliant results, the operation on the excluded pleura and atelectatic lung offers more consistent ones, as for instance in pleural

M. R. Demel, Wien, spoke on *Indications for a Free Introduction of a Piece of Bone in New Fractures and Pseudoarthrosis*.

Harry Platt, Manchester: *Bone Grafting in Recent Fractures and Pseudoarthrosis*.—(1) In recent fractures bone grafting is an ineffective method of securing internal fixation when compared with other forms of osteosynthesis such as plating. (2) The essential distinction between delayed union and true non-union must be recognized. (3) Delayed union is a temporary suspension of osteogenesis which, in the majority of cases, can be successfully treated by conservative methods. Premature operative interference is to be condemned. In certain circumstances union may be hastened by drilling the fragments at the site of the fracture. Additional osteogenetic stimulus may be provided by a limited type of bone graft in the form of an osteoperiosteal, sliding, spongiosa, or peg graft. (4) In true nonunion a bone graft is required to act as a mechanical strut, as a conductor of bone, and as a producer of bone. The tibial graft best fulfills these requirements in pseudoarthrosis of the long bones. (5) Two standard methods of insertion of the bone graft are of established value: (a) the inlay and (b) the onlay or massive graft. (6) In the compound injuries of civil life the two-stage operation used in the treatment of gunshot fractures is rarely necessary. (7) Failures after bone grafting are usually the result of technical faults, most of which are avoidable. The main causes of fracture are (a) infection, (b) inadequate contact between graft and host bone, and (c) insufficient immobilization. In a graft used to bridge a long gap, absorption or spontaneous fracture may occur in spite of an efficient technique. (8) The least favorable sites for successful grafting are the shaft of the femur, lower third of the tibia, and lower third of the humerus.

Papers on bone grafts were discussed by the following:

Mm. R. Alessandri, Rome; O. Haberland, Cologne; Fr. de Quervain, Berne; R. Danis and F. Jonckheere, Brussels; J. de Fourmestaux, Chartres; D. Ferey, Saint-Malo; M. Zahradnick, Praha; L. and F. Berard, Lyons; A. Lambotte, Antwerp; R. Fontaine, Strasbourg; R. Zanoli, Pietraligure; Fr. Cleret, Chambéry; Gonzalez-Aguilar, Barcelona.

*Symposium on the Surgical Treatment of Cysts and Tumors of the Lung*: M. F. Sauerbruch, Berlin, gave the introduction.

M. H. Constantini, Algiers: *Physiological Conditions of Pulmonary Surgery*.—Increased knowledge of the physiopathology of the pleuropulmonary system required during recent years has altered our methods and made possible new operations on the lung. Pneumothorax is generally tolerated well by vigorous and healthy young subjects. It is the shock of the collapse which calls out the vago-sympathetic reflex capable of arresting the heart beat. The pulmonary elasticity, by allowing a sudden contraction, is responsible for these reflexes. Pressure anesthesia, today made possible thanks to the nitrous oxide apparatus and intratracheal anesthesia, counteracts the sudden collapse of the lung. Atropine, by paralyzing the vagus, and ephedrine, by stimulating the sympathetic, also mitigate the effects of collapse. The exposed lung easily chills and the patient therefore must be constantly warmed during operation. Bronchial effusions may be abundant and may obstruct the bronchial tubes, even to the point of asphyxia. The cough reflex, which evacuates them, therefore must be carefully maintained. The patient is operated on in the inclined position for the same reasons. Ligature of the hilar bronchus does not generally have any immediately serious consequences. Postoperative pneumothorax will eliminate sudden collapse reflexes, while oxygen therapy will eliminate asphyxia.

# REVIEW OF THE FORTY-SEVENTH FRENCH CONGRESS OF SURGERY, OCT. 17-22, 1938, PARIS\*

ADOLPHE JUNG, M.D., STRASBOURG, FRANCE

(From the Faculty of Medicine and the Surgical Clinic of Professor René Leriche)

**M. CHARBONNEL** (Bordeaux) and **A. Sicard** (Paris): **Treatment of Recent Closed Fractures of the Spine.**—The first part of this report is devoted to the radiologic examination of the vertebral column, the authors emphasizing the necessity of performing this procedure in such a way as to reveal best the region involved.

**M. Charbonnel: Treatment of Fractures of the Spine Without Nerve Complications.**—

I. The four following methods are discussed: (1) Novocain infiltration (Leriche): Twenty to thirty cubic centimeters of 1 per cent novocain are injected bilaterally at a point opposite the lateral surfaces of the fractured vertebral body. The infiltration relieves vasomotor disturbances, ameliorates pain, and permits immediate active motion. (2) Functional method without reduction (Magnus): Absolute immobilization and reduction are not necessary. The patient is placed in the dorsal decubitus position for four weeks (without any attempt at reduction) and then active motion is encouraged. Two weeks later he is permitted to walk. (3) The functional method with reduction and plaster cast (Böhler): This method is modified after the procedure of reduction described by Davis (1929), Roger (1930), and especially Watson Jones (1931). Attention is directed to the fact that the principle of this treatment is the association of reduction and physical therapy. The well-known technique of Böhler, i.e., reduction in the ventral position, is described. After demonstrating that fractures in the dorsal region or above cannot be reduced in the ventral position, the dorsal decubitus position, commonly employed in France, is presented. The advantages of this latter method are that it is better tolerated and permits better reduction. The duration of immobilization varies from three to six months, depending upon the gravity of the case. Physical therapy must be used also. No serious nerve complication has been reported following this method of reduction. (4) Operative methods: Open reduction is justifiable only in the case of fracture dislocation with displacement of the articular facets in which combined hyperlordosis and continuous extension are not successful in reduction. The use of bone grafts (Albee, Halsted, Leriche) has been employed for immobilization either immediately after the occurrence of the fracture or later.

II. *Indications and Results of Treatment of Dorsolumbar Fractures (D<sub>11</sub> to L<sub>5</sub>).*—In fractures of the dorsolumbar area with slight displacement most authors consider attempted reduction unnecessary and advocate immobilization in the horizontal position for one to two months and the subsequent wearing of a light cast for several months. Others, however, prefer getting the patient up early, emphasizing the value of immediate active motion (Leriche uses repeated novocain infiltration for this purpose). Even in these cases, Böhler advocates reduction and application of a cast in hyperlordosis followed by physical therapy for six to seven weeks while wearing the cast. It should be added that other authors (De Beule and Schatte, and Constantini) have suggested prophylactic bone grafts even in slight fractures.

\*Translated by Michael DeBakey, M.D., from Department of Surgery, School of Medicine, Tulane University, New Orleans, La.  
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*plombierung*. The simplest type of *plombierung* is that achieved by plugging with gauze. The author recommends following up the opening and evacuation of the cyst by superficial tubular drainage of short duration.

Autochthonous cysts do not lend themselves to a detailed critique, so far as results are concerned. In principle the cysts may be said to be susceptible to a mode of treatment similar to that used for echinococcal cysts. Multiple cysts necessitate lobectomy or pneumonectomy.

The following offered discussions: Mm. T. Edwards, London; R. Alessandri, Rome; A. Young, Glasgow; S. Santy, Lyons; P. Cokkalis, Athens; C. Eggers, New York, N. Y.; A. A. Altounyan, Aleppo; S. de Dziembowski, Bydgoszcz; J. M. Mason, Birmingham, Ala.; R. Monod, Paris; Cl. Crafford, Stockholm; P. Wertheimer, M. Berard, and M. Dargent, Lyons; R. Chiarolanza, Naples; J. Divis, Praha; R. dos Santos, Lisbon; P. Valdoni, Rome; A. von Miorini, Shanghai; H. Paschoud, Lausanne; A. Trias-Pujol, Barcelona; G. Petrescu, Ploesti; Dervis Manizade, Istanbul; E. Lourat, Bordeaux; A. L. d'Arreu, Cardill; H. Fruehaud, Angers; G. Potoschnig, Venice; S. W. Harrington, Rochester, Minn.; M. Iselin, Paris; T. H. Sellors, London; M. Dargent, Lyons; Ch. Mayer, Brussels.

unrecognized and disfiguring fractures in young infants may be the origin of scoliosis appearing in adolescence. Children over 7 years of age may be treated in the same manner as adults, but bone grafts should be used very cautiously until the twentieth year.

**A. Sicard: The Treatment of Fracture of the Spine With Nerve Complications.—**

I. The author discusses first the anatomic, osseous, meningeal, and cord lesions, calling attention to the fact that marked osseous displacement does not necessarily indicate severe nerve lesions. Whereas extradural hematoma, being diffuse, does not usually produce compression of the cord, subdural hematoma, being localized, easily causes compression. One of three mechanisms may cause the development of a spinal cord syndrome: (1) vasomotor disturbances, (2) compression by fragment of bone or by hematoma, and (3) partial or total destruction of the spinal cord.

II. *The clinical manifestations* are not pathognomonic of each type of cord involvement. An incomplete paralytic syndrome, occasionally produced by slight cord involvement, almost always represents radicular lesions. On the other hand, in the presence of complete paralysis no clinical sign is pathognomonic of complete involvement of the cord. This can be determined subsequently with the rapid development of trophic changes, such as decubitus over the sacrum and heels and early and persistent priapism. Of the laboratory procedures, such as electric stimulation and lipiodol instillation and roentgenography, only the latter is important and of therapeutic significance in demonstrating the presence of a fragment of bone or an apophyseal articulation projecting into the spinal canal.

III. *The Methods of Treatment.*—(1) Absolute conservatism in addition to respiratory exercises and massage is advocated by some authors. The results are not convincing. Of 79 total paraplegias reported by Magnus, there were only 4 complete recoveries. (2) Reduction of the fracture which has certain advantages and is not dangerous except in the presence of impaction of the articular processes, in which case it is absolutely necessary first to release the impaction before attempting reduction in hyperlordosis. The role which reduction of the fracture may play in the development of cord lesions is considerable in certain cases. (3) Laminectomy which the author neither advocates nor discards routinely.

IV. *The Author Presents the Following Therapeutic Steps.*—(1) Do not remain inactive. (2) Orthopedic reduction except in severe shock, then (3) in partial paralysis, if pain persists after several days, laminectomy is advisable. (4) In complete paralysis, if spastic paraplegia is present (which is exceptional), reduction usually relieves the nerve involvement. If flaccid paralysis is present and no amelioration has occurred in one to two weeks, laminectomy should be done.

*Discussion.*—Schotte (Ghent) emphasizes the usefulness of epidural or paravertebral anesthesia in the treatment of nerve root disturbances following fractures of the spine. Jacobovici (Bucharest) reports personal observations. Oltramare (Geneva) discusses Kümmel-Verneuil syndrome which should be avoided by proper treatment. Ch. Mayer (Brussels), on the basis of 86 personal cases, is of the opinion that reduction has considerable advantages in simple fractures as well as in those with nerve complications. Olgenick (Amsterdam) emphasizes the importance of repeated lumbar punctures in certain cases. Edema, which may produce signs similar to anatomic section, causes only transient block of from eight to twelve days. If the block does not disappear, laminectomy is necessary. Leriche (Strasbourg) observes that, whereas it is generally agreed that immediate reduction should be done in cases of moderate severity, there is divergence of opinion as regards its value in the very severe cases. In benign cases and those in which reduction is contraindicated he uses novocain infiltration which has considerable advantages. In cases with nerve complications, unimproved after re-

The results of these various methods in slight fractures without displacement are good if the treatment is well applied and the patient is under constant surveillance. Permanent disability in cases in which the classical method (immobilization) is used is approximately between 10 and 20 per cent; whereas, in those treated by the Böhler method it is 0 to 10 per cent. Definite conclusions cannot be made regarding the treatment by novocain infiltration because of the insufficient number of cases but the results appear excellent.

In compression fractures of the dorsolumbar region the classical method of immobilization without reduction gives bad results in from 39 to 76 per cent of the cases. The method of Böhler seems to be of particular value in these cases because it has reduced these bad results to about 20 per cent. However, 30 per cent of the good results develop secondary compression. Early bone grafts without reduction give results which are better than those following the classical method and somewhat similar to those of Böhler. Early grafts after reduction and the use of physical therapy would appear the most advantageous, but the number of cases is too small to determine this. According to the author, early bony graft is formally indicated in: (1) comminuted fractures, (2) multiple fractures, (3) oblique fractures showing progressive displacement following reduction and application of plaster cast, and (4) fracture dislocations particularly with fracture of the posterior arch. It is also indicated in spondylolisthesis.

III. *Treatment of Dorsal Fractures (D<sub>1</sub> to D<sub>10</sub>).*—The treatment used in fractures of the dorsolumbar region as described above is applicable also to fracture of this region. However, reduction in the dorsal position is more advantageous in this region. According to the author, the results obtained by the Böhler method (only 11.5 per cent bad results) are in contrast to those obtained by the classical method (43 per cent bad results). Considering the fact that secondary compression is particularly more frequent in dorsal fractures, early bone graft is indicated here, especially in fractures of several adjacent vertebrae.

IV. *Cervical Fractures (C<sub>3</sub> to C<sub>7</sub>).*—In recent cervical fractures with displacement, most surgeons attempt reduction by constant traction (2 to 3 kg. of weight). This requires several hours or days and must be controlled by roentgenography, following which immobilization is obtained by a plaster cast.

The danger of secondary displacement is the most important consideration in the treatment of fractures of the cervical vertebrae. This is observed not only in unrecognized and untreated fractures but also in those in which reduction and application of cast have been done. Severe nerve complications may occur. (According to Soto-Hall, of 17 reduced cervical fractures there were 5 with secondary paralysis.) If reduction cannot be obtained, some authors advocate immobilization and bone graft when signs of secondary displacement appear. Others advise either immediate graft or after three to four weeks have elapsed. The author cannot make definite conclusions regarding the advisability of doing routine immediate bone grafts or doing grafts when displacement increases because in the two cases treated respectively in this way the late results were practically the same.

V. *Fractures of the Atlas and the Axis.*—These fractures are treated along the same principles as the preceding type of fractures. Reduction is obtained by constant traction. Bone graft is not performed routinely but done when a fracture-dislocation is insufficiently reduced or when secondary displacement occurs.

VI. *Multiple Fractures.*—In multiple fractures, occurring at different and distant levels, treatment consists of reduction in the dorsal position and in applying the support in the region of the most severe fracture. In cases of slight multiple fractures, therapy is functional with novocain infiltration.

VII. *In infants under 6 years of age,* treatment by classic immobilization with constant vigilance is sufficient. Prolonged surveillance is essential because certain

C. The chronic forms may be of embolic origin or follow an acute phase, of variable intensity, and sometimes of short duration. The metastatic manifestations may continue after the acute stage. Numerous and dispersed, these metastatic localizations occur in various sites, but are elective in the bones, the joints, and the connective tissue. They progress to abscess formation and the purulent contents constantly reveal the same type of staphylococci. Repeated blood cultures will demonstrate the existence of septicemia.

II. *Biologic Aspects of Staphylococcic Septicemia*.—The authors call attention to the fact that experimental staphylococcic septicemia in animals does not give the same pathologic manifestations that are observed clinically. However, it demonstrates certain facts: (a) that the route of propagation of infection is essentially venous, (b) that the infection may persist even after removal of the primary focus, and (c) that the staphylococci release a powerful and lytic toxin possessing lethal properties toward all the cells of the body, although by inoculation it can produce an active antitoxin.

In the circulation the staphylococci have a tendency to aggregate in contact with or in the interior of platelets or leucocytes. Whereas some are destroyed by this means, others, instead of being attacked, are actually protected. The organisms thus carried in the circulation may be eliminated in the bile, urine, and intestinal contents and in this process are apt to be altered (Fliessinger). Upon encountering the various elements of the reticuloendothelial system, the staphylococci produce destructive or necrosing and pyogenic lesions which are manifested in the following successive stages: microbic embolus, inflammatory reaction in the region of the thrombosed vessels, miliary abscess in the zone of infiltration. Aside from the cellular reaction, the staphylococci are destroyed by a humoral reaction (opsinins of Wright, stimulins of Metschnikoff, bacteriophage of F. D'Hérelle).

The author then concisely discusses the factors which cause a staphylococcic infection, such as a simple furuncle, accompanied by bacteremia as shown by positive blood culture but not a true septicemia, to be transformed suddenly under certain conditions into a true septicemia. Among these is the eventual toxicity to the organism and the development of virulence of the staphylococci which has long been considered but difficult to demonstrate. Other factors concern the biologic state of the host: intoxication, mistakes in therapy, avitaminosis, deficiency in hepatic and renal function, disturbance in sugar metabolism, and acidosis. The clinical behavior, the rarity of complete recovery, and the tendency to relapse of staphylococcic infections probably depend upon these fundamental factors.

P. Moiroud: *The Treatment of Staphylococcus Septicemia*.—The author states that, in spite of the primary clinical gravity of septicemia with diffuse suppurative localization, spontaneous recovery may occur unless there is involvement of the heart or brain. He considers the following types of therapy:

1. *Proper Means of Improving the General State*.—Transfusions, especially immunotransfusions, have given favorable results although difficult to evaluate. Shock therapy (using colloidal metals), which should not be employed in weak patients or those presenting myocardial disturbances or involvement, has had some success. Intravenous injections of carbon increases leucocytosis, stimulates the reticuloendothelial system, and seems to have an absorptive action on the toxin, but its practical efficacy is not certain. Vitamins, especially vitamin C, are particularly valuable.

2. *Treatment by the Products of Bacteria*.—Vaccinotherapy may be a double-edged weapon (Bazy). Useful in certain cases, in others it may stimulate the infection and increase its spread. The greater the virulence of the infection, the more attenuated the vaccine should be (Grégoire). Vaccinotherapy has been employed most in the osseous forms of staphylococcic septicemia. The results are impossible



duction, routine laminectomy is performed, preceded by cystostomy. Lambotte (Anvers) endorses the conclusions of Leriche as regards the efficacy of routine laminectomy in paraplegias. Laminectomy is never dangerous and an operative death has not occurred in 30 cases. Four cases saved by operation are presented briefly. Fontaine (Strasbourg) presents 7 cases with bone graft fixation in which the late results were excellent. In most of these the vertebral column is not ankylosed, is absolutely painless, and there is practically no disability. In cases of cord complications, he is in agreement with his chief, Professor Leriche, that laminectomy should be done almost routinely. Five of 11 operative cases were very much relieved, if not completely. Jung (Strasbourg) presents 3 cases treated by novocain infiltration in the clinic of his chief, Professor Leriche. The osseous lesion was slight in one case, the second case was a very old woman, and the third case was a very obese woman. These represent the three essential indications of novocain infiltration. The results are excellent. Attention is directed to his work with Brunschwig (Chicago) which showed the significance of the sensitive innervation of the articulation of the vertebral bodies. Mallet-Guy (Lyon) describes his technique of treating fractures of the spine. Lambert (Lille) states that he has obtained excellent results in 20 cases by reduction in hyperlordosis in the dorsal position, which he has employed since 1922. Patel (Lyon) emphasizes the fact that restoration of function is based on the anatomic lesion. P. Wertheimer (Lyon) calls attention to the usefulness of lipiodol instillation and the harmlessness of laminectomy. Sénéchal and Hamel (Paris) describe numerous techniques. Delchef (Brussels) selects the type of treatment most adaptable to the individual case. Roeder (Paris) calls attention to the difficulty of roentgenographic diagnosis in certain cases in which anomalies of the vertebrae may resemble fractures. Chavannaz (Bordeaux) emphasizes the frequency and severity of unrecognized fractures of the spine. Grinda (Nice) is of the opinion that the orthopedic treatment is efficacious and adequate in the majority of fractures of the spine. Delageniere (Le Mans) and Arnaud also took part in the discussion.

J. Patel (Paris) and P. Moiroud (Marseilles): *Clinical Forms and Surgical Treatment of Staphylococcic Septicemia.*—

J. Patel: I. *Clinical Aspects.*—The author describes the characteristic features of staphylococcic septicemia. The primary focus is usually in a wound or in a cutaneous infection, such as a furuncle. Other foci may be in the mucosal surfaces (angina or rhinitis), in puerperal or postportal infections, or in the genitourinary tract. Once septicemia exists, distant secondary foci are extremely frequent.

A. There are essentially two acute types of staphylococcic septicemia: (1) The type which appears as an acute infectious disease and the real diagnosis is determined only after the presence of staphylococci in the blood stream is established. Whereas in the fulminating form death occurs in three to five days, in the acute form the duration is from eight to twelve days. (2) The type in which the etiology is obvious. In this form the author considers the "malignant staphylococcic infections of the face" with secondary septicemia and the forms with early metastatic manifestations clinically appearing three to four days following the original infection. In those cases in which metastasis to bone (osteomyelitis) occurs or to the cutaneous region (purulent pustulous exanthemata) the infection can be attributed usually to the staphylococcic organisms.

Laboratory procedures demonstrating the existence of staphylococci in cutaneous pustules, in urine, and in blood establishes the definite diagnosis in these forms.

B. The subacute types are most common. After a period of frank septicemia, there is an apparent gradual subsidence towards recovery during which there appear evidences of localization most frequently in joints, bone, connective tissue, muscle, lung, and kidneys.

therapy may be employed with success in toxic diseases, it may not be valuable in diseases having a local virulent action. At present it is realized that the staphylococcus produces a toxin but staphylococcal infections are not essentially toxic diseases. Staphylococci may possess two pathogenic factors. From a surgical standpoint, respect should be shown the protecting wall surrounding a focus of infection. J. Leveuf (Paris) classifies osteomyelitis from a septicemic standpoint into two groups: (1) those in which blood cultures are positive in 57 per cent of the cases during the first two or three weeks (during this period intervention is contraindicated) and then become negative and the temperature drops; osseous changes become visible roentgenographically on the twelfth day; (2) those in which blood cultures remain positive and fever persists until death; these cases are true septicemia with osseous localization. R. Leriche (Strasbourg) states that the explanation for the development of septicemia on the basis of "increased virulence of staphylococci" is theoretical. Invasion of the microorganisms is actually due to lessened resistance of the host. Thus an infection which was previously latent or saprophytic may suddenly become pathogenic as a result of various excesses or exhaustion on the part of the host. Therapeutic investigations should be considered with this objective in mind. In this connection avitaminosis may be an important factor.

Others who took part in the discussion are: L. Sauvé (Paris), Jeanneney (Bordeaux), F. Papin (Bordeaux), M. Vanlande (Arinée), P. Lombard (Algiers), M. Arnaud (Marseille), L. Arnaud (Saint-Etienne), and P. Ulrich (Paris).

P. Maulouguet (Paris) and Pollosson (Lyon): **Sarcoma of the Muscles and Connective Tissue of Extremities.**—This report is based on a study of malignant tumors of the extremities originating in muscle or in connective tissue which surrounds the muscles, nerves, and vessels. In this manner the authors include tumors of the soft parts and the vessels of the extremities as well as tumors having various histologic terms, such as myxoma, malignant lipoma, lipomatous myxoma, and rhabdomyoma. The term, tumors of the soft parts of extremities, is particularly bad, because from the present study there are excluded tumors of: connective tissue of skin, synovial bursae, lymphatic ganglia, nerves, and vessels. One hundred and nineteen cases of sarcoma of muscles and connective tissue of extremities were studied histologically and classified as follows:

(1) Sarcoma of mesenchymal cells	8
(2) Fibroblastic sarcoma	38
(3) Lipoblastic sarcoma	33
(4) Rhabdoblasic sarcoma	13
(5) Osteoblastic sarcoma	5
(6) Angioblastic sarcoma	16
(7) Giant cell sarcoma	6
(8) Superficial sarcoma (these are similar in character to the above types but originate superficial to the subcutaneous fascia and are relatively more benign)	10
(9) Myxofibrocytoma	7
(10) Xanthogranuloma	2

Careful anatomic study of these tumors reveals that they are apparently well encapsulated, including neighboring tissue as vessels, nerves, muscles, and bone only as adjacent structures. However, the connective tissue capsule does not necessarily indicate limitation of the growth. Leriche emphasizes the fact that neoplastic cells may be found in the connective tissue outside the capsule.

These tumors invade neither the vessels nor the nerves. Whereas sarcomatous cells infiltrate the periarterial tissue and the adventitia, they never extend to the

to evaluate. The toxoids (Ramon) induce, in animals as well as in man, the formation of a specific antitoxin readily demonstrable in the serum. Aside from this, there exists in the serum a natural antitoxin of weak potency, produced by the staphylococcal infection. But it should be realized that a toxoid of high titer is not necessary for clinical recovery. Actually these investigations are in their incipency and successes alternate with failures. The bacteriophage (d'Hérelle), according to certain authors, has a veritably heroic action. Sauvé employs it intravenously in desperate cases.

3. *Chemotherapy*.—The intravenous injections of mercurochrome (Young), acriflavine, and alcohol have had some success. Intra-arterial injections have been particularly efficacious in infections of an extremity. However, this does not displace local surgical therapy. Intracardiac injections (Leriche) of mercurochrome have been employed in two cases with transitory improvement. Intrafocal injections of antiseptics are of no value.

4. *Surgical Treatment*.—Surgical intervention, such as total excision of the atrium of infection, would appear logical, but it is more theoretical. It is impractical in malignant staphylococcal infections of the face. It may consist in certain cases of amputation of an extremity. But in most instances it is too late. Venous ligation, in an attempt to prevent the release of organisms into the general circulation, is valuable in certain cases but its practical usefulness is limited. Osseous localization must be considered seriously as regards therapy. The methods of intervention are incision, trephining, and resection. Early resection, known in France since Vigarous (Montpellier, 1761) and Ollier (Lyon, 1861), has been abandoned because of the danger of nonregeneration of bone. However, it has been applied recently with some success following the observation of Hallopeau (1922). Subsequently Levent championed primary diaphyseal resection but at present he is more conservative.

In malignant staphylococcal infections of the face absolute conservatism is generally agreed upon. In cases of extension, ligation of the angular vein to prevent progression into the cavernous sinus has been advocated and performed but the majority of French surgeons, in contrast to their foreign colleagues, consider its advantages with considerable doubt.

Genitourinary localizations are the result of elimination of the micro-organisms by the kidney which occurs early and constantly. Perinephritic phlegmon, pyelonephritis, and prostatic abscess originate in this manner. The latter frequently opens spontaneously into the ureter, but surgical intervention may be necessary. Heitz-Bayer has approached these infections endoscopically. Subacute or chronic epididymitis, in certain cases, necessitates epididymectomy. The therapeutic indications in puerperal septicemia are very difficult to determine. Staphylococcal myositis is frequent especially in those cases in which vitamins B and C are lacking. Incision and resection are logical interventions. The author also calls attention to hepatic and pleuropulmonary localization, and to the occurrence of arterial emboli.

In conclusion the author emphasizes the usefulness of correlating all methods of therapy, the importance of not discarding general treatment, the revival of chemotherapy, and the present status of the delayed evacuation of metastatic collections.

*Discussion*.—R. Debré (Paris) calls attention to the definition of septicemia as conceived by Nicolle, which is based upon the presence of three factors: the presence of grave clinical manifestations indicating a severe infection, the existence of metastatic localizations, and the occurrence of numerous microorganisms in the blood. Bacteremias are frequent and occur especially in the terminal phase of malignant staphylococcal infections of the face and in osteomyelitis. Whereas these are not true septicemias, the borderline is not definitive. Whereas specific biologic

## Book Reviews

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**Surgical Diseases of the Mouth and Jaws.** By Earl C. Padgett. Cloth. Pp. 807, with 334 illustrations. Philadelphia, 1938, W. B. Saunders Company. \$10.

This well-written book will appeal in particular to three types of practitioners, the general surgeon, the plastic surgeon, and the dental surgeon. The author has attempted to bridge the gap between the domains of dentistry and surgery. The scope of the book, however, is considerably wider than its title would indicate. Extensive discussions of the management of the lymphatic areas of the neck tributary to epidermoid carcinoma of the mouth and face, the principles and application of irradiation in the treatment of malignant neoplasms, inflammations and diseases of the salivary and lachrymal glands, neuralgias and motor derangements affecting the face, mouth, and jaws, and diseases involving the neck enhance the value of the book considerably.

The dentist will find information which will enable him to detect lesions of the mouth earlier and more accurately. The general surgeon will find a clear delineation of the principles of treatment of those conditions which at the present time are properly treated only by the practitioner trained in both dentistry and surgery, of which there are not many. The plastic surgeon will find detailed discussions of practically all of the problems of reconstructive surgery having to do with the mouth and face. This portion of the book is profusely illustrated with both photographs and diagrams.

In general it can be said that the book is written in a conservative and orthodox manner. On subjects about which there may be debate, both sides of the question are presented and although the author frequently expresses his own ideas the reader is usually left to form his own opinion. The experienced surgeon will undoubtedly regret that the author does not express his own opinions more freely.

This book with its excellent illustrations, bibliography, and index can be well recommended to both student and practitioner.

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**Bile; Its Toxicity and Relation to Disease.** By O. H. Horrall. Cloth. Pp. 434. Chicago, 1938, The University of Chicago Press. \$4.

The author has summarized in 281 pages an extensive literature concerning the action of bile in health and diseased conditions. The bibliography alone covers more than 100 additional pages and contains more than 2,000 references.

It is pointed out by the author that one of the deterrents to more rapid progress concerning knowledge of the behavior of bile acids is lack of a wholly satisfactory chemical test for their presence. The author stresses the relative nontoxicity of bile pigments and indicates that bile acids are the essential toxic element in bile when biliary retention occurs or when bile escapes into abnormal locations.

A number of pathologic states bearing upon the physiology of bile are discussed, such as the hemorrhagic dyscrasias of jaundice, hemorrhagic pancreatic necrosis, bile peritonitis, jaundice, and external biliary fistula. The author summarizes the avail-

media of arteries. The vascularity of these tumors is usually very poor and according to the recent arteriographic studies of dos Santos the circulation of the tumors appears to be essentially venous. The lymphatics are almost always involved.

Sarcoma of muscles may be infiltrative or well encapsulated. It is important to realize that sarcoma of muscle as well as connective tissue can be osteoblastic and may be easily confused with tumors of osseous origin.

Metastasis is frequent and usually occurs in the pleuropulmonary region which was involved in 29 of the authors' cases. Certain benign connective tissue tumors, such as myxofibrocytomas, are difficult to distinguish even microscopically.

Clinically, sarcoma of the thigh occurs most frequently. It is usually well encapsulated, movable, not tender, and growing slowly. Functional disturbances as circulatory or nervous are remarkably absent for a long period of time. Adenopathy is also absent. Roentgenograms reveal the bone to be intact. Examination for distant metastasis, especially to the pleuropulmonary region, should be made.

The prognosis of these tumors is grave. They usually end fatally due to metastasis or after ulceration in the local area with secondary infection and cachexia. The prognosis is not good even in the treated cases. Of the 119 cases of the authors, 88 died, 15 recovered, and 16 are too recent to state results. Histologic study does not give definite significant information regarding the prognosis. Age is also of no prognostic significance.

Of the various methods of treatment, simple enucleation is to be condemned as recurrence practically always follows. Even total ablation is not satisfactory because it is too limited in scope. Amputation and disarticulation, except in late cases, are the only operative procedures which should be considered. The disarticulation should be either interscapulothoracic or interilioabdominal.

A considerable proportion of these tumors are radiosensitive. In a series of 45 cases the authors found 26 radioresistant and 19 radiosensitive. The histologic type determines this to some extent. Whereas certain forms of angioblastic and lipoblastic sarcomas are particularly radiosensitive, osteoblastic sarcomas and those of mesenchymal origin are radioresistant. Superficial sarcomas are less grave than the deep forms.

The authors report 15 total recoveries in their series of 119 cases. In addition to this there were 10 cases of superficial sarcomas with 6 recoveries. Of the successful cases, 5 were treated by local operation (undoubtedly these were not very malignant), 2 by amputation, and 10 by combined surgery and irradiation.

The authors make the following conclusions: (1) Whereas in the case of a small tumor total extirpation should be done rather than biopsy, in large tumors biopsy may be done but the laboratory report should be hurried. (2) Irradiation should be considered before surgical intervention as some tumors are radiosensitive. Even if the tumor is radioresistant, the loss of a few days is not significant. (3) In a large number of cases it will be necessary to resort to interscapulothoracic or interilioabdominal disarticulation.

The following took part in the discussion and in general agreed with the conclusions of the authors: Gordon Taylor (London), Louis Tixier (Lyon), J. Guyot (Bordeaux), A. Hamant (Nancy), and P. Ulrich (Paris).

career. One of these was Jacobson's *Operations of Surgery*; the other, Gerster's book on antiseptic principles of surgery. Kocher's *Operative Surgery* and Jacobson's *Operations of Surgery* have probably held a larger reading audience among English and American surgeons than any other similar books during their time. With the death of Professor Kocher in 1917, his work went out of print. Jacobson's work has been continued under the able directorship of successors at Guy's Hospital.

The general plan and format of the most recent edition of these two volumes follows closely that of the last publication. Some material has been added and some has been deleted. Only volume two on the abdomen has increased slightly in size. Ogilvie, Massie, A. Ralph Thompson, Gibberd, and R. C. Brock have revised and rewritten chapters in this new work.

One of the distinctive features of these volumes, the plan which is followed also in the eighth edition, is an adequate discussion of indications for operation, the choice of operative procedure, and the results both early and late of operation. In addition, pertinent references to literature are subtended at the bottom of the page. The illustrations in the main are quite satisfactory.

There is a wealth of information and experience summarized in these two volumes and any surgeon unfamiliar with them will do well to make their acquaintance.

More and more, however, it would appear that surgery in its manifold ramifications has become so broad that the writing of a complete work on operative surgery must of necessity become the task of a group of workers. When men write from their own experience, surgical barnacles drop out of texts of operative surgery and that which is best survives. One looks in vain through the text for information on some of the newer developments in surgery without satisfaction. Chapter 32 in volume two proposes to discuss some of the new things in surgery, but it is a poor and incomplete effort. This reviewer feels that if Jacobson's *Operations of Surgery* is to continue to enjoy the prestige which it has had for decades, subsequent editions must have more collaborators writing upon the field of their special interests.

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**The Synovial Membrane and the Synovial Fluid.** By David H. Kling. Cloth. Pp. 299, with 80 illustrations and 34 tables. Los Angeles, 1938, The Medical Press. \$5.

This little monograph deals with the anatomy and physiology of the synovial membrane and the state of the synovial fluid in joints in health and disease. It contains a large volume of information garnered from a number of sources. Practical chapters on the bacteriology of joint effusions, the technique of aspiration of joints and the injection of air into joints for purposes of diagnosis are included.

The author points out that the synovial fluid has normally a pH between 8.2 and 8.4, that it is in fact, next to pancreatic juice, the most alkaline fluid in the body. He also cites the susceptibility of articular cartilage to destruction with weak acid solutions. The capacity of the normal joint for absorption through the medium of the synovial membrane is pointed out.

The volume contains a great deal of useful information and needs to be read and studied to be appreciated. It can be recommended with enthusiasm to all those who have an interest in the physiologic behavior of joints.

able information upon these subjects. This reviewer had expected to find some mention of the work of Whipple and his associates, which indicates the great value of the feeding of bile to obviate bleeding in jaundice. The author feels that the toxic action of bile salts and the transudation of protein-containing fluid into the peritoneal cavity are the responsible lethal factors in bile peritonitis. He is inclined to regard the bacterial factor in bile peritonitis as relatively unimportant. Unfortunately a chapter on the relationship of the biliary constituents to cholecystitis or cholelithiasis is not included.

The volume is authoritative and modern; anyone wishing to orient himself in the general problem of the physiologic actions of bile will do well to make the acquaintance of this monograph.

**Athletic Injuries.** By Augustus Thorndike, Jr. Cloth. Pp. 208, with 104 illustrations. Philadelphia, 1938, Lea and Febiger. \$3.

This little monograph detailing the experience of the author over a five-year period in dealing with athletic injuries of Harvard athletes is an interesting and informative contribution. The author deals systematically with sprains, strains, dislocations, and fractures. In no sense does this text essay to discuss completely all the medical aspects of the various injuries. So little is known concerning the actual pathology of sprains and strains, that it would have been quite in order for the author, whose experience with them has been considerable, to debate upon them at length. He relates the experience of Leriche who exposed twice the tibiotarsal ligaments for sprain and found them intact; in consequence of this experience, Leriche believed that the disability of many so-called sprains was due largely to pain in the tissues about the tendons and came to inject novocain locally for relief of pain and loss of function. Whereas the author lends no factual proof, it is his belief that most sprains and strains are due to actual tears or ruptures of ligaments or muscle fibers. It is somewhat startling to learn that the author has employed the application of cold to the extent that phlebitis is a not uncommon accompaniment.

The author describes the physiology of exercise concisely and discusses, somewhat more briefly than the importance of the subject, the principles of therapy. A useful bibliography is appended. Surgeons who deal with athletic injuries and the minor accidents of industry will find this monograph useful.

**The Operations of Surgery.** By R. P. Rowlands and Philip Turner. Ed. 8. Cloth. Vol. I, pp. 1045, with 435 illustrations, 38 in color; Vol. II, pp. 998, with 514 illustrations, 4 in color. Baltimore, 1938, William Wood and Company. \$10 per volume.

A ten-year interval has elapsed since the appearance of the seventh edition of this well-known two-volume text on operative surgery. In the meanwhile a new publisher sponsors its appearance in the United States and the senior author has died. In 1889 W. H. A. Jacobson, of Guy's Hospital, a surgeon of great learning, introduced the work as a single volume. It proved at once a tremendous success and from that day to this, this life-work of Jacobson has been appreciated everywhere and has enjoyed a great prestige and wide usage among English-speaking surgeons. Dr. Wm. J. Mayo is said to have remarked that two books were constant companions and guides in the early days of his surgical

# SURGERY

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## Original Communications

### THE DISTENTION FACTOR IN SIMPLE INTESTINAL OBSTRUCTION

AN EXPERIMENTAL STUDY WITH EXCLUSION OF SWALLOWED  
AIR BY CERVICAL ESOPHAGOSTOMY

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*(From the Department of Surgery, University of Minnesota Medical School)\**

IT HAS become increasingly apparent that the factor of distention plays a significant role in the sequence of events which attends obstruction of the bowel. Up until about fifteen years ago, it was believed largely that absorption of abnormal toxins formed during the course of the obstruction was the important determinant which brought about a lethal issue. The breakdown of this hypothesis began with an understanding of the effects of dehydration and dechlorination which accompanied pyloric and duodenal obstruction or fistula.<sup>2, 3</sup> The demonstration of the efficacy of saline solution in prolonging the lives of dogs with duodenal obstruction served to make the significant lethal factor in high intestinal obstructions fairly well understood.<sup>4, 6</sup>

The cause of death in experimental ileal obstructions has defied complete understanding and has been the subject of considerable conjecture.<sup>9</sup> The administration of saline solution fails to prolong life materially in experimental ileal obstructions in dogs; whereas, obstruction of the pelvic colon in the dog may be survived for long periods of time without the administration of saline solution. Attempts have been made repeatedly in this laboratory to elucidate the mechanism of the lethal factor in experimental ileal obstructions.<sup>1, 10, 17</sup> It

\*Aided by a grant from the Graduate School of the University of Minnesota.  
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**Adventures in Respiration: Modes of Asphyxiation and Methods of Resuscitation.** By Yandell Henderson. Cloth. Pp. 316, with 15 illustrations. Baltimore, 1938, Williams and Wilkins Company. \$3.

The author has summarized in this monograph his ideas concerning the role of carbon dioxide in the control of respiration, asphyxia, and resuscitation of the newborn. Carbon monoxide asphyxia, mountain sickness, and acclimatization receive special consideration. The author believes that muscle tonus is a significant factor in initiating respiration at birth. Atelectasis accompanying operation, the author feels, is due in large measure to the depression of muscle tonus and particularly of the diaphragm which attends the administration of anesthesia.

There is much to commend in this volume and the surgeon, anesthetist, and obstetrician will find in it much useful information which he can apply practically.

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**The Surgery of Oral and Facial Diseases and Malformations. Their Diagnosis and Treatment Including Plastic Surgical Reconstruction.** By George V. I. Brown. Ed. 4, cloth. Pp. 778, with 1019 illustrations. Philadelphia, 1938, Lea and Febiger. \$10.00.

It may be said that there is a wealth of material in this book, so much so that a fair critical review hardly can be given. The feast of information begins with anesthesia in the first chapter, going through pathologic dentition, and includes a chapter on diseases of the nervous system of 113 pages with a color plate of photomicrographs of the gasserian ganglion. There are twenty-five chapters in all, with several on plastic surgery in the concluding pages that are more condensed. There are twelve color plates and many illustrations that are very good and clear. Some, however, are so small that the details cannot be made out. In the illustration of temporal muscle repair of a paralyzed face, the paralysis is shown on one side and the operative diagram on the other, which might prove misleading to some readers.

The statement is made that free skin grafts taken from another person will be satisfactory if both persons are of the same blood group. The fallacy of this, as far as our present knowledge of blood groups extends, is almost universally known, and, although it may have been an oversight, it is of enough fundamental importance to be somewhat unfortunate in a standard reference work.

In the preface the author indicates a wide range of readers to whom the book should prove valuable, and certainly it should to those who have worked with the author for it is a full summary of a long experience in this field of surgery.

digestive juices could be absorbed and obstruction of the terminal ileum be tolerated fairly well. It was with this premise in mind that we began in May, 1933, to study the effects of ileal obstruction in the dog with exclusion of swallowed air from the intestine by cervical esophagostomy.

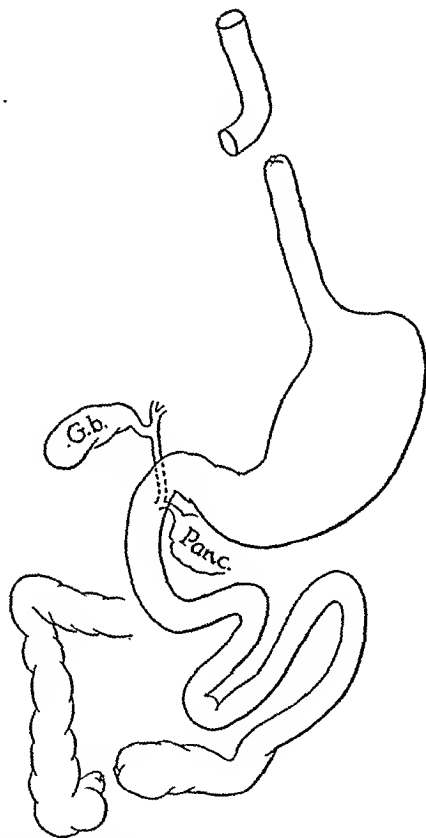


Fig. 2.—Cervical esophagostomy to exclude swallowed air. Complete ileal obstruction is tolerated well under these conditions and dogs survive for long periods when saline solution is given liberally subcutaneously. The gut is usually not distended at autopsy. The cause of death is starvation. It is necessary, however, to invert the distal end of the cervical esophagus, for if it is not occluded, the animals still swallow considerable quantities of air.

#### METHODS

A cervical esophagostomy was established in dogs by a two-stage operative procedure (intraperitoneal pentobarbital anesthesia, 35 mg. per kilogram of body weight) in which the esophagus was first isolated and elevated, a slip of the left sternocleidomastoid muscle being drawn beneath it. When the wound was well healed (usually in about a week), the esophagus was transected and both ends were brought out to the skin. For varying periods of time, lengthened as the investigation proceeded from one to two to four weeks, the dog was maintained by liberal feedings of the Scott-Ivy pabulum<sup>10</sup> administered by

has been our belief that inability to empty the lower reaches of the gut by vomiting causes it to become distended with ensuant sustained increments of intraluminal pressure attended in turn by interference with blood flow and satisfactory oxygenation. By severing the terminal ileum and anastomosing the proximal end to the stomach (end-to-side), it was found possible to keep a dog alive for fifty-six days (Fig. 1). In this animal the ileal content was returned to the stomach, from which vantage level it was the more readily evacuated by vomiting.<sup>17</sup>

Demonstration of the possibility of relieving certain mechanical intestinal obstructions by suction applied to an inlying duodenal tube lent credence to the belief that distention with its associated sequelae was the item of chief importance in causing death in ileal obstruction.

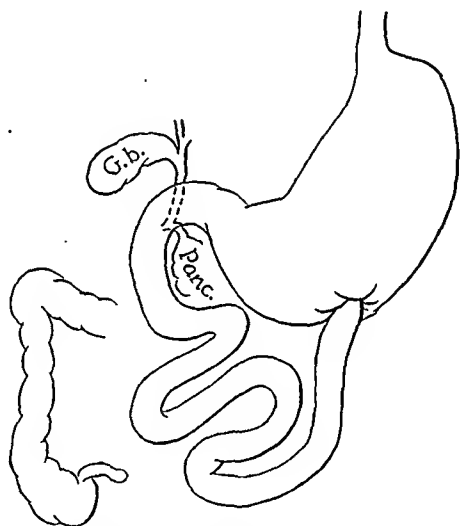


Fig. 1.—Dogs survive complete obstruction of the terminal ileum for 7 to 8 days. When saline solution is given subcutaneously, dogs survive 8 to 10 days; an occasional dog survives somewhat longer. Anastomosis of the terminal ileum to the stomach permits dogs to survive much longer (one animal survived 56 days). This operation obviates sustained increase of intraluminal pressure in the terminal ileum. A preliminary ileosigmoidostomy<sup>14</sup> before the establishment of ileal obstruction increases also the survival period. (Reproduced here from Wangenstein, O. H., and Leven, N. L.: *Arch. Surg.* 22: 658, 1931.)

The agents which cause distention are gas and the digestive juices. McIver and his associates<sup>8</sup> have shown swallowed air to be the principal source of gaseous distention of the stomach after abdominal operations. In this laboratory it has been shown that swallowed air accounts for about 68 per cent of the gas present in instances of simple mechanical obstruction.<sup>7</sup>

Having in mind the great absorptive capacity of the small intestine, it is quite reasonable to assume that, if swallowed air could be excluded from the intestine even in the presence of obstruction, the

TABLE I

## CONTROLS

OPERATION	DOG (NO.)	INITIAL WEIGHT (KG.)	SALINE SOLUTION (C.C.)	SURVIVAL (DAYS)	GAS (C.C.)	FLUID (C.C.)	WEIGHT AT DEATH (KG.)
A. Esophagostomy	28	12	0	7	Gut collapsed	Gut collapsed	9.6
	29	12	0	6	Gut collapsed	Gut collapsed	9.0
	30	10	0	6	Gut collapsed	Gut collapsed	4.0
	31	10	0	8	Gut collapsed	Gut collapsed	7.5
	14	7	0	4	Gut collapsed	Gut collapsed	5.0
	75	10	0	4	Gut collapsed	Gut collapsed	8.2
	No. dogs			Avg. Min. Max.	Avg. Min. Max.		% loss
	6			6 4 8	Almost none	Almost none	25
	Average				Almost none	Almost none	7.2
	B. Esophagostomy*	103	600	22	Almost none	Almost none	8.0
C. Terminal ileal obstruction	104	12	600	22	Almost none	Almost none	10.0
	105	16	600	10	Almost none	Almost none	% loss
	No. dogs			Avg. Min. Max.	Avg. Min. Max.		40
	3			18 10 23	Almost none	Almost none	12.5
	Average				300	200	12.0
	2	15	0	3	250	150	15.0
	3	15	0	7	700	400	8.0
	15	18	0	8	200	100	10.5
	17	10	0	10	300	150	8.0
	18	13	0	8	350	200	% loss
D. Terminal ileal obstruction + saline solution	19	10	0	12	350	200	16
	No. dogs			Avg. Min. Max.	Avg. Min. Max.		9.2
	6			8 3 12	350 200 700	200 100 400	11.5
	Average				400	300	13.0
	6	10	600	7	300	200	14.0
	7	12.5	600	5	350	250	8.5
	12	14	600	8	250	100	% loss
	13	15	600	8	200	100	7
	24	9.5	600	7	300	250	100
	No. dogs			Avg. Min. Max.	Avg. Min. Max.		400
	5			7 5 8	300 200 400	250 100 400	

\*The average survival period of three other dogs with esophagostomies given 1,000 c.c. of saline solution subcutaneously every day was 43 days.

catheter into the distal opening of the cervical esophagus. The weight loss of the dogs in the latter experiments in which esophageal feeding was maintained for four weeks after the establishment of the esophageal fistula was uniformly less than 10 per cent of the initial weight. Then, following a period of starvation of twenty-four hours, the terminal ileum was obstructed by dividing the gut and inverting both ends. On completion of the procedure, the distal end of the transected esophagus was inverted carefully. In the earlier experiments the distal end of the esophagus was left open, but it was learned quickly that such an animal swallowed as much air as a dog with the esophagus intact. The dogs were then maintained up until death by the daily subcutaneous administration of physiologic saline solution. In the earlier experiments 600 c.c. of saline solution was given once daily. In the latter experiments 1,500 c.c. was given daily in two divided doses. A few of the last dogs operated upon were transfused a few times with blood from other dogs in an attempt to increase the values for the plasma proteins which became lowered considerably by the prolonged period of starvation. To the final dog in the series, whose survival period was longest (Table III, Dog 11), the vitamins B<sub>1</sub>(1 mg.) and C(100 mg.) were given subcutaneously each day during the last three weeks of life. In addition, an intramuscular injection of 20 c.c. of a 10 per cent solution of glycine was given daily, and also daily retention enemas of 100 c.c. of 5 per cent aqueous dextrose solution and one ounce of cod-liver oil, which, however, were retained poorly. When it became apparent that the animal was moribund, he was killed with an intracardiac injection of ether. At the time of autopsy, the absence or presence of distention was noted and the amount of gas and fluid present was determined.

Control survival periods were determined for dogs with esophagostomy and for animals with obstruction of the terminal ileum given saline solution subcutaneously (Table I). Animals which developed infection in the cervical wounds were excluded in this consideration.

## RESULTS

The early results which have been briefly reported elsewhere<sup>15</sup> were disappointing. For, despite the finding of a gut which was usually collapsed save for a short segment immediately proximal to the obstruction, the survival period for the dogs with ileal obstruction upon which esophagostomy for the exclusion of swallowed air had been performed was found to be no longer than in the controls in which obstruction of the terminal ileum alone had been done and in which animals distention was a prominent feature. These early results in

long survival periods, which were obtained fairly uniformly in the latter experiments, would appear to have been starvation.

From an inspection of the tables, it is to be noted that esophagostomy diminishes notably the amount of gas and fluid found at necropsy as contrasted with the animals having ileal obstruction but no exclusion of swallowed air (compare Table I *C* and *D* with Table II *A* and *B*

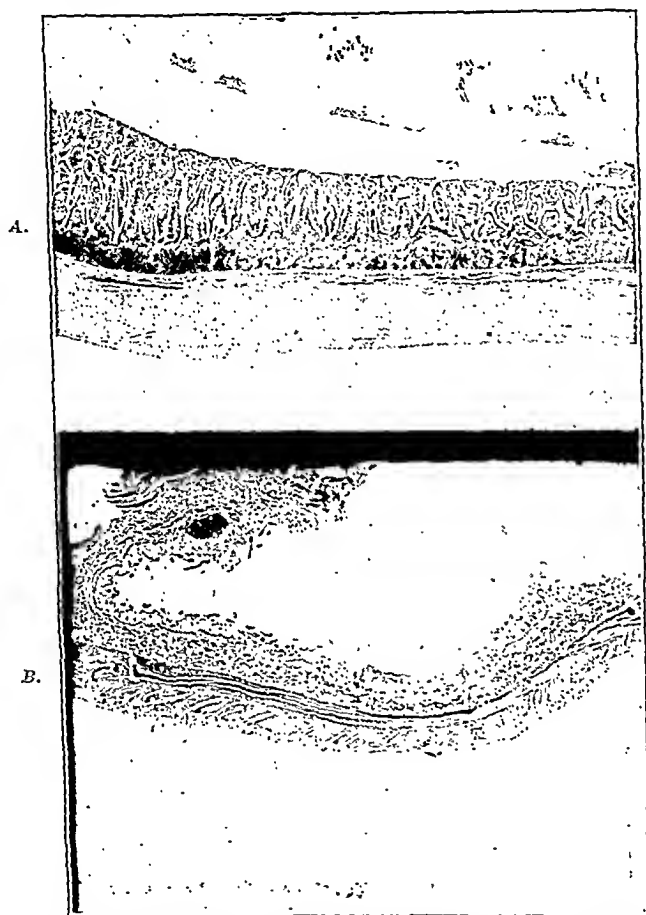


Fig. 4.—*A*, Photomicrograph ( $\times 12\frac{1}{2}$ ) indicating the hypertrophy of the muscle of the gut wall (near obstruction) as contrasted with *B*, the normal terminal ileum at a comparable level.

and Table III). In a few of the animals with long survivals (Table III) in which esophagostomy had been performed, a surprisingly large amount of fluid or gas and fluid was found in the obstructed bowel at necropsy. In two of these (Dogs 9 and 10) reasonable causes operated to bring the condition about. In Dog 9 a volvulus was brought about by rotation of the obstructed gut about an adhesive band; in the other, food had been present in the stomach at the time of opera-

which no direct correlation was obtained between the length of survival and the presence or absence of distention in the gut at necropsy left us somewhat confused with reference to the significance of the distention factor. However, in the light of the success which was attending conservative decompression of the obstructed bowel in man by suction applied to an indwelling duodenal tube, we were not ready to conclude that a "toxic factor" was responsible.



Fig. 3.—Photograph of the condition found at autopsy in Dog 11 (Table III). This animal survived complete ileal obstruction with cervical esophagostomy for 57 days. The terminal reaches of the gut are slightly distended. The entire closed loop of esophagus, stomach, and entire small intestine contained 125 c.c. of fluid and 100 c.c. of gas.

The earlier experiments were performed during the course of a very hot summer (1933). With gradual lengthening of the time between performance of esophageal fistula and establishment of obstruction in the terminal ileum (four weeks), with the more liberal administration of saline solution (1,500 c.c. of one per cent daily), avoidance of experimentation during the hot summer months, occasional transfusion of blood toward the end of the experiment, and use of only large and older dogs, it became apparent that when swallowed air was excluded from the bowel the obstructed gut could resorb effectually the digestive juices from the bowel. The cause of death in the animals with

TABLE III  
ESOPHAGOSTOMY AND OBSTRUCTION

OPERATION	DOG (No.)	INITIAL WEIGHT (KG.)	SALINE SOLUTION (C.C.)	SURVIVAL IN DAYS	GAS (C.C.)	FLUID (C.C.)	WEIGHT AT DEATH (KG.)	REMARKS
Esophagostomy + feeding for 1 month; then closure of the distal esophageal opening and terminal ileal obstruction + saline solution	1	24.0	1,500	19	100	150	16.5	Dogs 1-7 showed no distention of the gut except for segment 15 to 20 cm. proximal to ileal ob- struction
	2	20.0	1,500	20	150	50	16.0	
	3	17.5	1,500	32	0*	100	12.0	
	4	26.0	1,500	40	50	50	15.2	Dog 4 received 2 transfusions of
	5	15.9	1,500	29	0*	350	12.5	citrated blood, 300 c.c. each.
	6	17.0	1,500	45	50	60	11.5	Total plasma protein just be- fore death, 4.5 gm. %
	7	18.5	1,500	34	0*	90	10.0	Slight distention
	8	18.0	1,500	33	175	150	13.5	
	9	15.0	1,500	33	600	800	9.5	Died with a volvulus; gut mark- edly distended
	10	20.0	1,500	45	1,000	350	14.5	Stomach and jejunum are con- tracted; received 4 transfusions of citrated blood, 300 c.c. each, after ileal obstruction
	11	18.3	1,500	57	100	125	12.5	Ileum was distended and contained 500 gm. of semisolid fecal ma- terial; this dog received a total of 5 transfusions of citrated blood, 300 c.c. each, after the ileal obstruction; just before the animal was sacrificed, plasma protein 4.4 gm. %, plasma chlorides 676 mg. %, and nonprotein nitrogen 60.6 mg. %

\*Too small to be accurately measured.



TABLE II  
ESOPHAGOSTOMY + OBSTRUCTION

OPERATION	DOG	INITIAL WEIGHT (KG.)	SALINE SOLUTION (C.C.)	SURVIVAL (DAYS)	GAS (C.C.)	FLUID (C.C.)	WEIGHT AT DEATH (KG.)
A. Esophagostomy + terminal ileal obstruction	8	8.2	0	2	75	25	6.8
	9	10.4	0	2	100	180	8.5
	11	7.3	0	4	60	100	5.5
	20	13.0	0	4	65	40	11.6
	21	10.0	0	4	50	15	6.2
	22	9.5	0	2	40	20	7.5
	25	10.0	0	3	60	150	5.5
	26	11.5	0	2	30	40	8.0
	49	15.0	0	3	50	50	13.0
	73	13.5	0	4	100	50	11.6
No. dogs 10							
Average							
B. Esophagostomy + terminal ileal obstruction + saline	76	10.0	600	Avg. 3 Min. 2 Max. 4	Avg. 53 Min. 30 Max. 120	Avg. 67 Min. 15 Max. 150	9.5
	77	12.5	600	5	75	80	10.0
	78	9.4	600	4	85	100	8.2
	90	12.5	600	5	10	60	10.0
	91	10.0	600	6	120	100	7.2
	92	10.0	600	3	30	100	7.0
	93	13.0	600	5	210	80	10.5
	94	14.5	600	11	60	200	11.5
	95	10.0	600	5	100	630	6.8
	96	12.5	600	3	100	150	10.0
	80	15.0	600	5	35	210	13.0
	81	10.0	600	4	100	140	8.5
	82	10.0	600	6	80	200	8.5
	102	11.5	600	19	180	110	7.0
	106	10.0	600	16	60	200	8.5
	107	15.0	600	20	40	140	11.5

days has been reported. In man, as has previously been pointed out, however, complete obstruction of the colon not uncommonly terminates in perforation (and usually of the cecum) unless the obstruction is relieved by surgical decompression of the large bowel. Because of the competency of the ileocecal sphincter and because of the lengths of the lips of the valve, regurgitation into the lower reaches of the ileum frequently does not occur and a virtual closed loop obstruction ensues. It has been pointed out that such an obstruction may be unattended by vomiting and accompanied only by great distention and "gas pains." Despite the absence of fluid loss, such an obstruction is one of the most potentially hazardous of all simple obstructions.<sup>14</sup>

The results of the experiments here reported serve to shed light upon the somewhat enigmatic cause of death in obstructions involving the greater portion of the absorptive area of the gut. The majority of occlusions of the small intestine observed clinically concern its lower reaches in which the items of dehydration and dechlorination are not nearly so serious as in obstructions near the secretory level of the gut. Failure to prolong materially the survival of dogs with ileal obstruction by the parenteral administration of liberal quantities of saline solution has contributed considerably to general acceptance of the "toxic absorption factor" as the primary cause of death in ileal obstructions. Yet, the dog which possesses a relatively short small intestine may tolerate complete occlusion of the entire alimentary tract above it, if swallowed air is excluded. Exclusion of swallowed air permits such a segment even when obstructed to absorb the normal digestive juices. It is reasonable to assume that the same would hold true for man, particularly inasmuch as man has a relatively longer small intestine than the dog. At the same time, these experiments indicate the significance of increased intraluminal distention and tension (when swallowed air is not excluded). Evidence has been obtained which indicates that a sustained intraluminal pressure of 20 cm. of water, if maintained for twenty-two to twenty-eight hours, results in increased permeability owing to decreased viability of the gut wall. The avenue over which such abnormal absorption may occur in the presence of a damaged gut wall is probably the transperitoneal route,<sup>12</sup> though the experiments of Haerem, Dack, and Dragstedt with botulinus toxin would suggest increased absorption via normal avenues when the bowel is obstructed.<sup>5</sup>

#### SUMMARY

A method has been devised (cervical esophagostomy) by which ileal obstruction in dogs may be studied with exclusion of the swallowed air factor. In eleven such dogs (Table III) the average survival period

tion. In a previous study the nature of the gas found in the obstructed bowel, which was essentially a closed loop, was reported earlier. Seventy-five per cent of the gas was nitrogen, an indication that the more diffusible gases originating within the closed loop had been displaced largely by diffusion of nitrogen into the bowel lumen from the blood stream.<sup>7</sup>

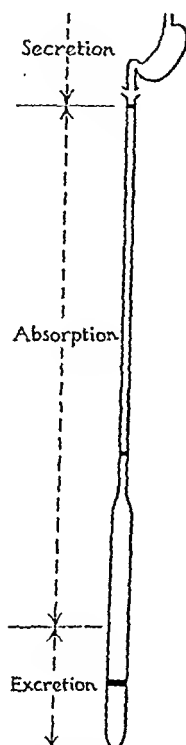


FIG. 5.—The intestine projected as a straight tube. The effects of obstruction at various levels are discussed in the text. (Reproduced here from Wangensteen, O. H., and Leven, N. L.: *Arch. Surg.* 22: 658, 1931.)

#### DISCUSSION

In Fig. 5 the gut is projected as a long straight tube. Obstruction of the gut in its upper reaches, where the digestive juices first enter it, is attended by essentially the same effects which accompany fistula at the same level. In either instance, and more effectually in obstruction than fistula, dehydration and dechlorination may be obviated by the liberal parenteral administration of water and sodium chloride. Whereas dogs with duodenal obstruction survive from two to four days ordinarily, if given generous amounts of saline solution subcutaneously, survival for as long as four weeks is not unusual.

Complete obstruction of the pelvic colon in dogs may be survived until the animal dies of starvation.<sup>16, 17</sup> Survival from forty to fifty

15. Wangensteen, Owen H.: *The Therapeutic Problem in Bowel Obstructions*, Springfield, Ill., 1937, Charles C. Thomas, Publisher.
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after the establishment of complete occlusion of the terminal ileum was thirty-six days. One dog survived for fifty-seven days. It was found that dogs in which a long closed loop of esophagus, stomach, and entire small intestine was made, absorbed the digestive juices when swallowed air was excluded. At autopsy the gut was usually found collapsed. The exclusion of swallowed air obviates the distention factor and in turn the sequelae of decreased viability and increased permeability which attend sustained increases of intraluminal pressure. These experiments indicate that complete occlusion of the terminal ileum may be well tolerated if the gut is not allowed to become distended by swallowed air. In effect, therefore, these experiments indicate that the mechanical factor of distention and not a "toxic factor" accounts for the lethal issue in ileal obstructions.

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suture anastomosis between the terminal ileum and the proximal transverse colon. Others (Lahey and his associates<sup>3</sup>) prefer an obstructive type of resection for lesions in either the right or left colon, the procedure being essentially a modification of the original Mikulicz operation. Still others (Rankin,<sup>4</sup> Pemberton and Whittaker,<sup>5</sup> and Allen<sup>6</sup>) advise a two-stage operation, consisting first of an anastomosis between the low ileum and the transverse colon, to be followed by right hemicolectomy some three to six weeks later.

The present study is concerned with the cases of carcinoma of the right colon observed in the University Hospital from 1925 to 1937 and was undertaken, first, in order to make a careful analysis of the symptoms, signs, and complications in order thus possibly to clarify the early clinical picture of the disease; second, to evaluate the worth of the different operative procedures from the standpoint of mortality and post-operative complications; and third, to learn the end results of surgical treatment, both radical and palliative operations being considered. During this twelve-year period, the records of 91 cases of carcinoma situated in that segment of bowel between the ileocecal junction and the proximal transverse colon were found suitable for study. In the majority of these cases the diagnosis was verified by operation or necropsy and in these instances, histologic confirmation of the diagnosis was usually available. A certain few cases in which neither operation nor necropsy was performed were included, providing there was convincing clinical evidence in support of the diagnosis. Thus some cases having a compatible history with an abdominal tumor mass or positive x-ray and laboratory findings were accepted for study when thorough examination had also served satisfactorily to exclude other lesions.

#### ANATOMIC LOCATION

Table I gives the exact situation of the lesion in the right colon in the 91 cases. The cecum, as in the reports of other observers, was the section most commonly involved, while cancers of the hepatic flexure were second in frequency. It has been noted (McGlannan<sup>7</sup>) that the incidence of carcinoma at the hepatic and splenic flexures of the colon is slightly

TABLE I  
CARCINOMA OF THE RIGHT COLON  
ANATOMICAL LOCATION

LOCATION OF LESION	NUMBER OF CASES	PER CENT
Cecum	54	59.4
Ascendens	9	9.8
Cecum and Ascendens	10	10.9
Hepatic flexure	14	15.5
Ascendens and hepatic flexure	2	2.2
Entire right colon	2	2.2
	91	100.0

## CARCINOMA OF THE RIGHT COLON\*

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FROM the standpoint of surgical diagnosis and treatment, carcinoma of the cecum, ascending colon, and hepatic flexure may be conveniently grouped under the general heading of carcinoma of the right colon. The clinical syndromes provoked by cancers in these several locations are essentially the same. They are frequently characterized by a severe secondary anemia even though there has been no visible loss of blood and also by the rarity of obstructive phenomena, both of which features stand in sharp contrast to the behavior of carcinomas of the left arm of the colon. Furthermore, carcinoma of the right colon is generally regarded as offering a better chance for cure than carcinoma at almost any other level of the digestive tract, this being due to the fact that these growths tend to remain localized for a long period of time. Metastasis to the regional lymph nodes and liver occurs at a relatively late stage in the life history of the disease, and, in this respect, the malignant growths of the right half of the colon differ considerably from cancers of the stomach, left colon, and rectum. Moreover, when surgical extirpation of a malignant lesion situated at any point in the right colon is to be performed, surgeons are quite generally agreed that right hemicolectomy is the procedure of choice. Cheever<sup>1</sup> mentions the following reasons for this: (1) Removal of a smaller segment of colon does not give a sufficiently wide margin of safety. (2) Due to the sacculated structure of the right colon and because it is devoid of peritoneum posteriorly, an anastomosis made here is less secure than one between the terminal ileum and the transversus, both of which are almost completely covered by peritoneum as well as being fairly mobile due to their respective mesenteries. (3) The ileum is provided with a good blood supply which minimizes the danger of suture-line necrosis with resultant leakage. (4) The operation is technically easier. Such a resection, of course, readily permits restoration of the intestinal continuity and a permanent artificial anus is not necessary. Concerning the exact details of the technique by which the operation can be best and most safely performed, there is no unanimity of opinion among different surgeons of considerable experience. Thus, some authors (Cheever,<sup>1</sup> Harvey<sup>2</sup>) favor a one-stage operation, consisting of resection of the right colon with a primary

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Since one of the purposes of the study was to summarize the significant symptoms and thus facilitate, if possible, earlier recognition of the disease, the chief symptoms of which these patients complained have been tabulated in Table III. It will be observed that some type of abdominal pain or distress was the most common chief complaint. The exact nature of the pain, its precise location, or the points to which it might radiate were neither constant nor characteristic and many variants of this complaint were noted.

TABLE III  
CARCINOMA OF THE RIGHT COLON  
CHIEF COMPLAINT

COMPLAINT	NUMBER OF CASES	PER CENT
Abdominal pain	37	40.6
Weakness	10	11.0
Abdominal pain and weakness	9	9.9
Diarrhea, abdominal pain and weakness	8	8.8
Constipation and abdominal discomfort	7	7.7
Tumor	6	6.6
Tumor and pain in right lower quadrant	6	6.6
Abdominal pain and vomiting	3	3.3
Abdominal distention and gas	3	3.3
No symptoms (accidentally discovered during routine examination)	2	2.2
Total	91	100.0
Appendectomy since onset of symptoms	10	11.0

Rankin states that the symptoms of carcinoma of the right colon may be divided into three main groups. The first is characterized by chronic digestive disturbances which tend to persist. Pain may be referred to the right upper quadrant of the abdomen, thus simulating chronic gall-bladder disease, or to the right lower quadrant simulating chronic appendicitis. The second group is composed of symptoms referable to anemia. Thus, weakness, dyspnea, and pallor without other symptoms may be noted. Finally, there is a smaller group, in which an abdominal tumor mass first discovered by the patient or by the physician during a routine physical examination is the first indication of trouble. Comparing this classification with Table III, we find that these cardinal symptoms which Rankin describes appear here either singly or in combination. The 6 cases with unusual symptoms, such as vomiting and abdominal distention, were cases in which obstruction was present and the symptoms were those of the complicating intestinal obstruction rather than of the carcinoma itself. Of particular interest are the last 2 cases in the table, neither of these patients having had any symptoms referable to the abdomen but both found to have a carcinoma of the cecum during the course of a searching examination. One patient had come to the hospital because of an orthopedic condition and the other because of a cutaneous disorder. Since nearly three-fourths of the patients had abdominal pain as the chief complaint and since it not infrequently was



higher than in the adjacent portions of the bowel. The slight narrowing of the lumen and consequent stasis at these points have suggested the factor of chronic irritation by intestinal contents as a possible etiologic agent. For purposes of orientation, it is of interest to note that, during a two-year period, Hodges,<sup>8</sup> of the Department of Roentgenology of the University Hospital, on the basis of x-ray examination found carcinoma of the colon distributed as follows: pelvic colon (rectum and sigmoid), 60 per cent; left colon (distal half of transverse and the descending colon), 18 per cent; right colon (cecum, ascending colon, and proximal transverse colon), 22 per cent.

Thus, while carcinoma of the left colon (sigmoid and rectum being included) is the more important lesion by virtue of its more frequent occurrence, carcinoma of the right colon is deserving of careful study, since Allen in his review of the Massachusetts General Hospital cases found the operative mortality to be higher in this group of cases than in the resections performed on the left side.

In Table II are shown the age and sex incidence. With regard to sex, nothing remarkable is noted, it being common experience to find males affected more frequently than females, and in this series the ratio was approximately two to one. The study of the distribution of the cases according to age revealed that nearly 85 per cent occurred in the so-called cancer age from 40 to 70 years, and only 10 per cent were found in persons under 40 years of age. This is in rather striking contrast to our recent experiences with carcinoma of the left colon, rectum, stomach, and breast, when a surprisingly large number have been observed in patients between 20 and 40 years of age.

TABLE II  
CARCINOMA OF THE RIGHT COLON  
SEX AND AGE INCIDENCE

SEX	NUMBER OF CASES	PER CENT
<i>Sex Incidence</i>		
Male	59	64.8
Female	32	35.2
Total	91	100.0
AGE	NUMBER OF CASES	PER CENT*
<i>Age Incidence</i>		
11-20 inclusive	1	1.1
21-30 inclusive	1	1.1
31-40 inclusive	7	7.7
41-50 inclusive	19	20.9
51-60 inclusive	28	30.8
61-70 inclusive	29	31.8
71-80 inclusive	6	6.6
Total	91	100.0

\*Mean, 55.22 years.

ease of cancer elsewhere and especially that of the gastrointestinal tract, is the rule, but unfortunately, because it is such a general symptom and one common to so many other chronic diseases, it does not assist greatly in arriving at an early diagnosis.

TABLE V  
CARCINOMA OF THE RIGHT COLON  
WEIGHT LOSS IN 82 CASES

NUMBER OF POUNDS	NUMBER OF CASES	PER CENT
No loss	5	6.1
1-10	7	8.5
11-20	19	23.4
21-30	20	24.4
31-40	14	17.0
41-50	6	7.3
51-60	2	2.4
61-70	2	2.4
71-80	0	0.0
81-90	0	0.0
91-100	1	1.2
Patient had lost weight but amount unknown (No record)	6 9)	7.3

Table VI gives the time interval between the onset of symptoms and the date of admission to the hospital. These data are of interest since one fact which we were anxious to learn was during what stage of the disease most of the patients were applying for surgical treatment. We find from this survey that 25 per cent of the cases were seen within the first three months following the onset of symptoms; 45 per cent, within six months; and 70 per cent, within a year.

TABLE VI  
CARCINOMA OF THE RIGHT COLON  
DURATION OF SYMPTOMS BEFORE ADMISSION IN 86 CASES

TIME	NUMBER OF CASES	PER CENT
Less than 1 mo.	4	4.6
1-3 mo.	18	20.9
4-6 mo.	17	19.6
7-12 mo.	21	24.4
13-18 mo.	6	7.1
19-24 mo.	13	15.2
25-36 mo.	4	4.6
Over 3 yr.	3	3.6
Total	86	100

*Clinical Findings.*—In the clinical examination the presence of an abdominal tumor is probably the most important physical sign. As shown in Table VII, such a tumor mass was discovered in 72 per cent of the cases. If reference is made to Table III, it will be noted that 12 patients, or 13 per cent of the group, actually gave the presence of an abdominal tumor mass as a chief complaint.

located in the right lower quadrant, it is perhaps not surprising that 10 patients, or 11 per cent of the group, had been subjected to appendectomy since the onset of symptoms and before hospital entry, a mistaken diagnosis of chronic appendicitis having been made.

A history of any change in the bowel habit of an individual is usually to be looked upon with suspicion, and, in teaching early diagnosis of cancer of the lower digestive tract, emphasis is placed upon the fact that any deviation from the normal for that individual, which tends to persist, calls for a thorough examination, including x-ray study by means of the barium enema. Such alterations in bowel habit may be in the nature of a tendency toward diarrhea or toward constipation. In our series, as far as could be told from a careful perusal of the case histories, no change in intestinal habit had been noted by the patient in half of the cases. Strangely enough, increasing constipation was considerably more common than diarrhea. The textbook symptom of alternating constipation and diarrhea was recorded in only six cases.

In the course of the routine history, patients were questioned specifically regarding any change in the appearance of the stools, and, as shown in Table IV, three-fourths of the patients denied having had bloody or tarry stools. This serves to emphasize the fact that a history of blood in the stool or on the stool is rarely obtained in cases of carcinoma of the right colon, and that a history of abnormal appearing stools is so uncommon that it will direct the attention of the examiner to the colon in only a small number of cases.

TABLE IV  
CARCINOMA OF THE RIGHT COLON  
SYMPTOMS

CHANGE IN BOWEL HABIT	NUMBER OF CASES	PER CENT
No change	44	48.3
Increasing constipation	24	26.4
Diarrhea	17	18.7
Alternating constipation and diarrhea	6	6.6
Total	91	100

ABNORMALITY OF STOOLS	NUMBER OF CASES	PER CENT
No change	68	74.7
Bloody	18	19.8
Tarry	5	5.5
Total	91	100

Table V presents the matter of weight loss in 82 cases in which the records were complete on that score. As might be expected, the great majority of patients had lost weight to some extent. As indicated in the table, in 65 per cent of the cases the amount of weight lost ranged between 10 and 40 pounds (4.6 to 18.2 mg.). Weight loss, then, as in the

TABLE VIII  
CARCINOMA OF THE RIGHT COLON  
BLOOD STUDIES

HEMOGLOBIN DETERMINATION	NUMBER OF CASES	ERYTHROCYTE COUNT	NUMBER OF CASES
15- 19	2	1.5-1.9	2
20- 24	4	2.0-2.4	3
25- 29	3	2.5-2.9	6
30- 34	2	3.0-3.4	9
35- 39	1	3.5-3.9	8
40- 44	8	4.0-4.4	14
45- 49	4	4.5-4.9	11
50- 54	9	5.0-5.4	3
55- 59	11	5.5-5.9	0
60- 64	9	6.0-6.4	1
65- 69	6	No record	34
70- 74	5	Mean 3.76	
75- 79	6		
80- 84	5		
85- 89	4		
90- 94	1		
95-100	2		
No record	9		
Mean 57.6			

such large raw surfaces constantly bathed in a fluid medium containing a concentrated culture of the most virulent organisms. Hence they conclude that there is nothing about the cecum or its mucous membrane which is essential to the hematopoietic system and that the explanation of the anemia lies in the presence of a large ulcerated surface from which blood can ooze and through which bacteria can enter. Rankin and Graham,<sup>12</sup> on the other hand, believe that the anemia is probably due to some perverted or inhibited function of the mucous membrane which allows toxins to be readily absorbed. In support of this contention they quote the work of Whipple, Schmidt, Koons, and others.

In order to determine whether the degree of anemia was an index of the extent of the lesion and therefore a criterion of operability, all cases explored surgically as well as those judged hopelessly inoperable when first seen were combined and divided into three groups, depending upon the hemoglobin readings. In 15 cases the hemoglobin was between 15 and 44 per cent; in 37 it was between 45 and 69 per cent; and in 22 it was over 70 per cent. The number of cases in which resection was possible in these three groups was 6, 20, and 10 respectively. Thus, as had been expected, the lowest resectability (40 per cent) was found in the group with the most severe anemia. However, in the middle group, with a hemoglobin range from 45 to 69 per cent, the operability was found to be the highest (54 per cent) while in the cases in which there was only a slight degree of anemia (hemoglobin 70 per cent or higher) the resectability was second highest (45 per cent). The best explanation for this seems to be that in this last group of cases there were some of

TABLE VII

CARCINOMA OF THE RIGHT COLON  
*Physical Examination in 86 Cases*

ABDOMINAL TUMOR	NUMBER OF CASES	PER CENT
Present	62	72.1
Absent	24	27.9
<i>Stool Examination in 31 Cases</i>		
OCCULT BLOOD	NUMBER OF CASES	PER CENT
Present	25	80.6
Absent	6	19.4
<i>X-Ray Examination in 82 Cases</i>		
	NUMBER OF CASES	PER CENT
Lesion demonstrated or suspected	72	87.8
Negative examination	10	12.2

Stool examinations were recorded in only 31 cases, but it is noteworthy that of this group the chemical tests for occult blood were positive in 80 per cent. This is of interest in view of the fact that, as was previously mentioned, 75 per cent of the patients gave no history of any gross abnormality of the stools.

Roentgen studies were made in 82 of the 91 cases and in 72, or 88 per cent, these were either positive for an intrinsic colonic lesion or the findings deviated from normal sufficiently at least to arouse the suspicion of the examiner and to raise the question of some abnormality in the bowel. Since this series of cases dates back to the time of the opening of the hospital in 1925, and in view of the great improvements in the technique of roentgen examination of the colon, it is probable that at the present time such a lesion can be demonstrated by a competent roentgenologist in at least 95 per cent of the cases.

Of the various laboratory examinations, the blood studies are of the chief interest. They are shown in Table VIII. It will be seen that a fairly marked anemia was present in most of the cases, as indicated by the mean hemoglobin reading of 57 per cent and the mean erythrocyte count of 3.76. In 1913<sup>9</sup> and again in 1921<sup>10</sup> W. J. Mayo pointed out that carcinoma of the right colon is more commonly associated with anemia than carcinoma of any other part of the body, with the exception of certain cancers of the stomach. Various explanations for this tendency to the production of anemia have been offered. Thus, it has been suggested that hemotoxins are formed; that the cecal mucous membrane is essential to a normal blood picture; that the anemia is related to the high degree of malignancy of these tumors; that it is associated with chronic intestinal obstruction, weight loss, or hemorrhage. This matter has been extensively studied by Alvarez and his associates. They find that there is a definite relationship between the area of the tumor removed at operation and the degree of the anemia and emphasize the fact that nowhere else in the interior of the body are ulcerating cancers found as large as those in the cecum. Furthermore, nowhere else are

TABLE VIII  
CARCINOMA OF THE RIGHT COLON  
BLOOD STUDIES

HEMOGLOBIN DETERMINATION	NUMBER OF CASES	ERYTHROCYTE COUNT	NUMBER OF CASES
15- 19	2	1.5-1.9	2
20- 24	4	2.0-2.4	3
25- 29	3	2.5-2.9	6
30- 34	2	3.0-3.4	9
35- 39	1	3.5-3.9	8
40- 44	8	4.0-4.4	14
45- 49	4	4.5-4.9	11
50- 54	9	5.0-5.4	3
55- 59	11	5.5-5.9	0
60- 64	9	6.0-6.4	1
65- 69	6	No record	34
70- 74	5	Mean 3.76	
75- 79	6		
80- 84	5		
85- 89	4		
90- 94	1		
95-100	2		
No record	9		
Mean 57.6			

such large raw surfaces constantly bathed in a fluid medium containing a concentrated culture of the most virulent organisms. Hence they conclude that there is nothing about the cecum or its mucous membrane which is essential to the hematopoietic system and that the explanation of the anemia lies in the presence of a large ulcerated surface from which blood can ooze and through which bacteria can enter. Rankin and Graham,<sup>12</sup> on the other hand, believe that the anemia is probably due to some perverted or inhibited function of the mucous membrane which allows toxins to be readily absorbed. In support of this contention they quote the work of Whipple, Schmidt, Koons, and others.

In order to determine whether the degree of anemia was an index of the extent of the lesion and therefore a criterion of operability, all cases explored surgically as well as those judged hopelessly inoperable when first seen were combined and divided into three groups, depending upon the hemoglobin readings. In 15 cases the hemoglobin was between 15 and 44 per cent; in 37 it was between 45 and 69 per cent; and in 22 it was over 70 per cent. The number of cases in which resection was possible in these three groups was 6, 20, and 10 respectively. Thus, as had been expected, the lowest resectability (40 per cent) was found in the group with the most severe anemia. However, in the middle group, with a hemoglobin range from 45 to 69 per cent, the operability was found to be the highest (54 per cent) while in the cases in which there was only a slight degree of anemia (hemoglobin 70 per cent or higher) the resectability was second highest (45 per cent). The best explanation for this seems to be that in this last group of cases there were some of

the less differentiated or more malignant tumors, which tended to metastasize early or to infiltrate extensively, while in this group also were found some of the smaller tumors which showed complications, such as perforation or obstruction at an early date. Hence, in general, it would seem that a severe degree of anemia denotes an advanced and often an inoperable lesion, but the degree of the anemia and the resectability do not run entirely parallel with one another.

TABLE IX  
CARCINOMA OF THE RIGHT COLON  
RESECTABILITY IN RELATION TO DEGREE OF ANEMIA IN 74 CASES

HEMOGLOBIN READING	NUMBER OF CASES	NUMBER OF CASES RESECTABLE	PER CENT
15-44	15	6	40.0
45-69	37	20	54.0
70-100	22	10	45.4

*Treatment.*—Table X shows in outline form the disposal which was made of the 91 cases. In 15 the lesion was thought to be operable but operation was refused. These patients either refused treatment entirely or went elsewhere. Eight cases were frankly inoperable and no treatment of any kind seemed worthwhile. Thirty-two cases, at the time of laparotomy, were found to have extensive infiltration into adjacent structures, hepatic or other distant metastases, or various conditions contraindicating any radical procedure. In 5 of the 32 the operation consisted of simple exploration with biopsy when possible. In 20 an ileocolostomy between the low ileum and the transverse colon was performed. In 2 ileosigmoidostomy was necessary because of involvement of the transverse colon. The 5 instances of enterostomy or cecostomy were advanced cases of acute intestinal obstruction and emergency operation was performed for the relief of the obstruction.

TABLE X  
CARCINOMA OF THE RIGHT COLON  
OPERABILITY

TREATMENT	NUMBER OF CASES	PER CENT
Operation advised; patient refused	15	16.4
Inoperable	8	8.8
Palliative operation	32	35.2
Ileotransverse colostomy	20	22.0
Ileosigmoidostomy	2	2.2
Cecostomy and enterostomy	5	5.5
Exploration only	5	5.5
Radical operation (resection)	36	39.6
Resection with primary suture anastomosis	25	27.5
Obstructive resection	6	6.6
Two-stage operation	5	5.5
Total	91	100.0
Resectability in 76 cases = 47.6%		

Resection was possible in 36 cases and if the 15 patients who refused treatment are disregarded, the resectability was 47.6 per cent. Undoubtedly in the group of 15 who refused treatment there were some favorable cases. Thus it seems reasonable to suppose that the resectability for the entire group was approximately 50 per cent.

The 20 palliative ileotransverse colostomies were all side-to-side lateral anastomoses. In some of these cases a proximal catheter enterostomy was added as a form of safety valve for the purpose of relieving tension on the suture line. More recently this practice has been abandoned, as it is now regarded an unnecessary precaution. As shown in Table XI, the mortality was considerably higher when the enterostomy was performed. The reason for this was usually some form of infection, either general peritonitis, or severe wound sepsis which often resulted in a persistent fecal fistula. Thus, we believe that the complementary proximal enterostomy in such cases is not only unnecessary but unwise.

TABLE XI  
CARCINOMA OF THE RIGHT COLON  
PALLIATIVE OPERATIONS

TYPE OF OPERATION	NUMBER OF CASES	LIVED	DIED	MORTALITY PER CENT
Ileotransverse colostomy	20	14	6	30.0
Lateral anastomosis without proximal enterostomy	13	11	2	15.4
Lateral anastomosis with proximal enterostomy	7	3	4	57.0
Ileosigmoidostomy	2	1	1	50.0
Cecostomy and enterostomy	5	1	4	80.0
Exploration only	5	4	1	20.0

The high mortality of 80 per cent in the small group of cases in which enterostomy or cecostomy was performed is not surprising. These were all far-advanced cases, and an attempt was made to relieve the acute obstruction even though the risk was great.

The radical operations fall into three main groups: (1) resection of the right colon with some form of primary suture anastomosis; (2) obstructive resection; and (3) a two-stage operation, consisting of ileotransverse colostomy as the first stage, followed by right hemicolectomy, after the function of the anastomosis was well established, usually about three weeks later.

In the first group of one-stage operations, with primary suture anastomoses, the anastomosis was of the side-to-side variety in 12, end-to-end in 9, and end-to-side in 4. In the two latter types a proximal enterostomy was always performed. This was also done in 6 of the 12 lateral anastomoses, while in the remaining 6 it was not thought necessary. Here again, the experience was the same as in the group of palliative side-tracking operations, i.e., the results were much superior when an enterostomy was not done. We, therefore, believe that if a one-



the less differentiated or more malignant tumors, which tended to metastasize early or to infiltrate extensively, while in this group also were found some of the smaller tumors which showed complications, such as perforation or obstruction at an early date. Hence, in general, it would seem that a severe degree of anemia denotes an advanced and often an inoperable lesion, but the degree of the anemia and the resectability do not run entirely parallel with one another.

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45-69	37	20	54.0
70-100	22	10	45.4

*Treatment.*—Table X shows in outline form the disposal which was made of the 91 cases. In 15 the lesion was thought to be operable but operation was refused. These patients either refused treatment entirely or went elsewhere. Eight cases were frankly inoperable and no treatment of any kind seemed worthwhile. Thirty-two cases, at the time of laparotomy, were found to have extensive infiltration into adjacent structures, hepatic or other distant metastases, or various conditions contraindicating any radical procedure. In 5 of the 32 the operation consisted of simple exploration with biopsy when possible. In 20 an ileocolostomy between the low ileum and the transverse colon was performed. In 2 ileosigmoidostomy was necessary because of involvement of the transverse colon. The 5 instances of enterostomy or cecostomy were advanced cases of acute intestinal obstruction and emergency operation was performed for the relief of the obstruction.

TABLE X  
CARCINOMA OF THE RIGHT COLON  
OPERABILITY

TREATMENT	NUMBER OF CASES	PER CENT
Operation advised; patient refused	15	16.4
Inoperable	8	8.8
Palliative operation	32	35.2
Ileotransverse colostomy	20	22.0
Ileosigmoidostomy	2	2.2
Cecostomy and enterostomy	5	5.5
Exploration only	5	5.5
Radical operation (resection)	36	39.6
Resection with primary suture anastomosis	25	27.5
Obstructive resection	6	6.6
Two-stage operation	5	5.5
Total	91	100.0
Resectability in 76 cases = 47.6%		

and often stormy. The added hazard of the administration of two anesthetics and the danger of postoperative complications in two post-operative periods have probably been greatly overemphasized in the past. It is true, of course, that the malignant growth is left in situ, during the interval of two or three weeks between stages, and, theoretically at least, it is capable of giving rise to metastases during this time. However, in view of the slow rate of growth of these colonic cancers, with metastasis taking place at a late stage of the disease, no great harm seems likely on this score. Furthermore, as the result of putting the tumor-containing bowel segment at rest by means of the ileocolostomy, there is a marked subsidence of infection, and the tumor mass may decrease in size so that its subsequent removal becomes safer and easier.

The optimal interval of time between the two stages is generally believed to be about three weeks; i.e., a sufficiently long period to allow the anastomosis to become firmly healed and its function well established. As to the time when the maximum degree of immunity of the peritoneum is attained, there is considerable difference of opinion. At the present time we are attempting to show when this occurs in experimental animals and these results will be the basis of a separate publication.

As indicated in Table XII, the lowest operative mortality followed the use of the two-stage operation. In this small group of cases there were two patients over 70 years of age, one 71 and the other 78, and both of them made a satisfactory convalescence. Furthermore, since this study was completed, 5 additional cases have been treated by this method with successful outcome, thus improving considerably the results shown in the table. We now believe that the two-stage operation should not be reserved for the poor surgical risk, but that it is the preferable procedure for most patients with malignant disease. Undoubtedly there are some patients who are able to withstand a one-stage operation

TABLE XII  
CARCINOMA OF THE RIGHT COLON  
RADICAL OPERATIONS

TYPE OF OPERATION	NUMBER OF CASES	LIVED	DIED	MORTALITY PER CENT
Resection with primary suture anastomosis	25	17	8	32.0
Lateral anastomoses	12	9	3	25.0
Lateral anastomoses without enterostomy	6	6	0	0.0
Lateral anastomoses with enterostomy	6	3	3	50.0
End-to-end anastomosis (with enterostomy)	9	7	2	22.2
End-to-side anastomosis (with enterostomy)	4	1	3	75.0
Obstructive resection	6	4	2	33.3
Two-stage operation	5	4	1	20.0
Total	36	25	11	30.06

stage resection is to be performed the strongest possible type of anastomosis should be employed in order to avoid the necessity of a complementary enterostomy. Such an anastomosis is undoubtedly the side-to-side type.

In this group of cases adequate statistical data are not available with reference to the relative merits of the different so-called aseptic types of anastomosis. In nearly one-half of the cases the anastomosis was made according to the Parker-Kerr basting-stitch technique or with the aid of the Furniss clamp. In the remainder of the cases an open anastomosis was performed. It is our belief, however, that the aseptic type of anastomosis has much to recommend it, and we continue to employ it when technically feasible.

While most surgeons are agreed that obstructive resection is a suitable procedure for lesions in the left colon, relatively few advocate its use on the right side. The chief objection to its use here is the fact that, during the interval between the actual resection and the time when the temporary intestinal fistula can be closed, the patient is handicapped by a complete ileostomy. While it may not be a serious argument against the use of this method, nevertheless the excoriation of the skin and the uncontrollable watery discharges are far more distressing and incapacitating than in the case of a temporary sigmoid or transverse colostomy. In the present series the number of patients treated by this method is so small that statistical data are of little value. However, in the figures available for comparison, the mortality proved to be essentially the same as for the one-stage resections, that is, approximately 32 per cent.

Likewise, the two-stage operation was utilized in only a small number of cases, and hence our experience with this procedure is limited. It is a method which has long been advocated by Rankin for patients who are not first-class surgical risks, and its various advantages have recently been emphasized by Pemberton and Allen. The chief reasons for employing a two-stage procedure are: first, that the amount of operating done at any one time is considerably decreased; and second, that the preliminary ileocolostomy confers upon the peritoneum a certain degree of immunity to infection so that the hemicolectomy can be done more safely. As Pemberton has pointed out, the first stage of the procedure is quite effective in sealing off the left side of the abdomen by adhesions. Thus, the second stage can be done with scarcely any exposure or handling of the small intestine. The added safety made possible by this method seems to more than compensate for any disadvantages that it may have. Most important of these disadvantages is probably the longer period of hospitalization. In spite of a two-stage procedure, however, the total number of hospital days is not greatly increased because the convalescence following each stage is usually smooth and uneventful; whereas, in the one-stage operation it is apt to be prolonged

peritoneum with interrupted silk sutures and of the fascia with either silk or the Babcock alloy steel wire, in our hands, have been very gratifying.

In Table XIV are listed the important complications of the disease which were present at the time of hospital entry. The incidence of obstruction, either acute or subacute, was somewhat higher than had been expected. When obstruction was present, it was usually due either to a large cecal growth so situated as to occlude the ileocecal junction, thus producing small intestinal obstruction, or else it was an advanced carcinoma situated at or near the hepatic flexure.

TABLE XIV  
CARCINOMA OF THE RIGHT COLON  
PATHOLOGY

COMPLICATIONS	NUMBER OF CASES	PER CENT
Perforation with abscess	2	2.2
Perforation with general infection	2	2.2
Acute or subacute intestinal obstruction	10	11.0
Duodenocolic fistula	1	1.1
<i>Incidence of Metastasis to Regional Lymph Glands in 25 Specimens</i>		
Glands involved	11	44.0
Glands not involved	14	56.0

The matter of regional lymph node involvement is of interest, since it is commonly believed that carcinoma of the cecum, for example, metastasizes at a later date than carcinoma elsewhere in the digestive tract. Important observations have been made by Craig and MacCarty,<sup>14</sup> Hayes,<sup>15</sup> and MeVay.<sup>16</sup> In 300 sections of colon resected for carcinoma, these authors isolated and studied microscopically the included lymph nodes. They found an increasing tendency for the lymph nodes to be involved in passing from the cecum to the rectum. Thus, the regional glands were positive in 47 per cent of the rectal cancers; whereas, involvement was present in only 32 per cent of the cecal growths. In the case of lesions situated between these two points, there was a fairly even gradation in metastasis. While complete records of nodal involvement were not available in all of the cases in the present study, microscopic examination of the regional lymph nodes was made in 25 of the resected specimens. The glands were uninvolved in 14, or 56 per cent, and positive in the remaining 11, or 44 per cent.

Table XV shows the end results of palliative ileocolostomy in the 15 patients upon whom this operation was performed and who were discharged from the hospital alive. It was possible to trace all of the cases and all had died.

The exact duration of life following operation is given in Table XVI. Whether such palliative operations are worth while depends considerably upon the circumstances and the problems presented by the individual case. It is certainly true that an average postoperative life expectancy

and this is particularly true when the resection is done for some lesion other than carcinoma. However, these are the exceptional cases and require very careful selection.

Table XIII gives the cause of death in all of the radical operations ending fatally. While general peritonitis was present in about one-half of the cases, it alone was not responsible for the fatal outcome as frequently as one might suppose. With greater standardization of the operative procedures and a fairly long meticulous preoperative preparatory regime, the incidence of general peritonitis has been very greatly reduced. Fatal cardiovascular or renal disorders were not uncommon. A considerable number of the deaths were due to those postoperative complications, especially pulmonary, which are common to all major

TABLE XIII  
CARCINOMA OF THE RIGHT COLON  
CAUSE OF DEATH FOLLOWING RADICAL OPERATIONS

	AUTOPSY
Resection with primary suture anastomosis	
Case 1. Pneumonia, wound sepsis	+
Case 2. Pneumonia, wound sepsis	+
Case 3. General peritonitis	+
Case 4. Paralytic ileus, cardiac failure, pneumonia	+
Case 5. General peritonitis	-
Case 6. Peritonitis, pneumonia	-
Case 7. Erysipelas, uremia	-
Case 8. Transfusion reaction	-
Obstructive resection	
Case 1. Gangrene ileal stump, general peritonitis, pneumonia	+
Case 2. Coronary occlusion	+
Two-stage operation	
Case 1. General peritonitis, pneumonia	+

surgical procedures carried out in patients of this age group. While the use of spinal rather than inhalation anesthesia may assist in reducing the incidence of postoperative pneumonia, probably more important is the constant attention to minute details in the postoperative care. Thus, encouraging the patient to cough, frequent changes of posture, hyper-ventilation by means of carbon dioxide inhalations, and the avoidance of too tight abdominal dressings are all points worthy of attention. Wound sepsis is an important postoperative complication and when it occurs in these debilitated patients, it not infrequently results fatally. On the basis of the experimental studies on vitamin C deficiency and wound healing made by Lanman and Ingalls,<sup>12</sup> Allen recommends the use of cevitamic acid and of liver extract intramuscularly both before and after operation, in order to favor normal wound healing.

We have been impressed with the rather marked decrease in the incidence of infected laparotomy wounds following the use of nonabsorbable suture material. Thus, in this type of case the results of closure of the

peritoneum with interrupted silk sutures and of the fascia with either silk or the Babcock alloy steel wire, in our hands, have been very gratifying.

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TABLE XVII  
 CARCINOMA OF THE RIGHT COLON  
 PATIENTS STILL LIVING FOLLOWING RADICAL OPERATION

Case 174403 is alive at the end of	3 mo.
Case 391863 is alive at the end of	6½ mo.
Case 389384 is alive at the end of	10 mo.
Case 390943 is alive at the end of	10½ mo.
Case 192307 is alive at the end of	11 mo.
Case 348964 is alive at the end of	2 yr., 9 mo.
Case 297753 is alive at the end of	3 yr., 3 mo.
Case 335881 is alive at the end of	3 yr., 4 mo.
Case 248994 is alive at the end of	4 yr., 1½ mo.
Case 303540 is alive at the end of	4 yr., 9 mo.
Case 262022 is alive at the end of	6 yr., 4 mo.
Case 226372 is alive at the end of	8 yr.
Case 187393 is alive at the end of	10 yr.

are not brilliant, nevertheless, the fact that one patient was found to be living and well at the end of ten years and another at the end of eight years shows that cure is possible by radical surgery. Of the 13 patients still living, 3 have survived for more than five years. Thus there were five-year cures in 12 per cent of all of the radical operations performed, or 3.3 per cent of the entire group of 91 cases.

#### SUMMARY AND CONCLUSIONS

1. The case records of 91 cases of carcinoma of the right colon observed in the University Hospital, during the twelve-year period from 1925-1937, have been reviewed and analyzed.

2. Carcinoma of the right colon was considerably less common than of the left colon. Over one-half of the cancers of the large bowel were found to be situated in the sigmoid and rectum. In the right colon carcinoma was considerably more common in the cecum than in the ascendens or hepatic flexure.

3. Males were affected more frequently than females, the ratio being approximately two to one. Over 80 per cent of the cases occurred in individuals between 40 and 70 years of age. The mean age was 55.22 years.

4. Some form of abdominal pain or discomfort was the most common chief complaint. Because of pain located in the right side of the abdomen or in the right lower quadrant, 10 patients, or 11 per cent of the group, had had appendectomies performed prior to admission to the hospital.

5. Approximately one-half of the patients gave no history of change in bowel habit. One-fourth complained of increasing constipation. Only 6.6 per cent gave a history of alternating constipation and diarrhea. Likewise three-fourths of the patients gave no history of abnormal appearing stools.



TABLE XV

## CARCINOMA OF THE RIGHT COLON

## END RESULTS OF PALLIATIVE OPERATION IN 15 CASES (ALL TRACED)

LIVED	NUMBER OF CASES	PER CENT
Less than 3 mo.	3	20.0
3- 7 mo.	6	40.0
7-10 mo.	5	33.3
Over 10 mo.	1	6.7
	15	100.0
Average length of life following operation		6.6 mo.
Longest survival period		20 mo.
Shortest survival period		1½ mo.

of 6.6 months is not very much to hold out in the way of hope, yet the temporary symptomatic improvement often noted, the protection against acute obstruction, and the frequent improvement in the anemia as well as occasional survival periods of 1½ to 2 years, would seem to justify the procedure. It is of interest to place upon record these results as in this clinic we have been engaged for some time in conducting a survey of the end results of the various palliative operations for the different types of abdominal carcinoma. We have now accumulated such data for carcinoma of the stomach,<sup>17</sup> pancreas,<sup>18, 19</sup> and rectum.<sup>20</sup>

TABLE XVI

## CARCINOMA OF THE RIGHT COLON

## END RESULTS OF RADICAL OPERATIONS IN 25 CASES (ALL TRACED)

LIVED	NUMBER OF CASES	PER CENT
6 mo. or less	1	4.0
7-12 mo.	1	4.0
13-18 mo.	1	4.0
19-24 mo.	4	16.0
25-30 mo.	1	4.0
31-36 mo.	1	4.0
Over 3 yr.	3	12.0
Still living	13	52.0
	25	100.0
Longest survival period of patients now dead		4 yr.
Shortest survival period of patients now dead		4½ mo.
Average survival period of patients now dead		26¼ mo.

It was likewise possible to follow all of the patients upon whom radical operations were performed. Half of the patients were found to be still living, and in the case of those who had died the average duration of life was 26½ months. The deaths were all checked with the vital statistics of the State Department of Health. While it is quite possible that death was due to causes other than recurrence, in a certain few of the cases, as a rule the circumstances of death as recorded on the death certificates leave little doubt that death was due either to a recurrence of the disease or to distant metastases. While these results of treatment

19. A follow-up study of the 25 radical operations showed that 12 patients were dead, in all probability due to recurrence of the disease. The average survival period for this group was 26½ months. Of the patients still living and well, there were 3 five-year cures; i.e., 12 per cent of the radical operations performed, or 3.3 per cent of the entire group of 91 cases.

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6. Nearly all patients gave a history of weight loss. In 65 per cent of the cases the amount ranged from 10 to 40 pounds (4.6 to 18.2 kg.).

7. Approximately 25 per cent of the patients came to the hospital within three months following the onset of symptoms; 45 per cent, within six months; and 70 per cent, within one year.

8. An abdominal tumor mass was noted on physical examination in nearly three-fourths of the cases.

9. In the group of 31 cases in which the guaiac and benzidine tests were performed, occult blood was found in the stools in 80 per cent.

10. Of 82 cases examined roentgenologically, the lesion was demonstrated or its presence was suspected in 88 per cent.

11. The mean hemoglobin reading for the group was 57 per cent. The mean erythrocyte count was 3.76.

12. The degree of the anemia was not necessarily a criterion of resectability. The lowest resectability occurred in the cases with the most marked anemia (15 to 44 per cent Hg). The highest resectability was found in the intermediate group (45 to 69 per cent Hg).

13. Palliative operations were performed in 32 cases, or 35.2 per cent of the group. Radical operations were possible in 36 cases, or 39.6 per cent. The resectability in 76 cases (excluding 15 patients who refused operation) was 47.6 per cent.

14. The most useful palliative operation was ileotransverse colostomy for the purpose of excluding the involved bowel segment and preventing obstruction in the future. The operative mortality in 20 cases was 30.0 per cent. The mortality was considerably higher when a proximal catheter enterostomy was performed simultaneously than when it was omitted.

15. Among the radical operations, while the number of cases in any one group is too small to make statistical comparisons of great value, the two-stage operation seems to be superior to any form of one-stage procedure, judging from operative mortality (20 per cent). Obstructive resections and one-stage resections with primary suture anastomoses, in general, carried about the same mortality; viz., 33 per cent.

16. Perforation of the bowel was a relatively uncommon complication, occurring in only 4.4 per cent of the cases. Acute or subacute intestinal obstruction, on the contrary, was somewhat more frequent than had been anticipated. It was noted in 10 cases, or 11 per cent of the group.

17. In 25 resected specimens in which microscopic study of the regional lymph nodes was made, metastases were found in the regional lymph nodes in 44 per cent, while the glands were uninvolved in 56 per cent.

18. A follow-up study of the 15 palliative short-circuiting operations showed the average duration of life following operation to be 6.6 months. The longest period of survival was 20 months and the shortest 1½ months.

most frequent causative agent of pancreatitis. In the remaining 40 per cent of cases lymphogenous, hematogenous, or ductal spread of infection must be considered. Vascular injury will also produce pancreatitis, as will physical trauma. The protected position of the organ lessens the danger from trauma, but many interesting cases of rupture and repair are reported.

*Incidence.*—Acute pancreatitis is a rare disease. From 1916 to 1937, inclusive, there were 268,293 patients admitted to the Henry Ford Hospital and of this number only 26 were operated upon for acute pancreatitis. Thus, there was only 1 patient with acute pancreatitis for each 10,000 admissions.

*Seasonal Incidence.*—Acute pancreatitis does not appear to have the definite seasonal variation that is demonstrable in so many diseases. The incidence by seasons of our cases is shown in Table I.

TABLE I  
ACUTE PANCREATITIS  
SEASONAL INCIDENCE

SEASON	NO. OF PATIENTS	PERCENTAGE
Spring	8	30.8
Summer	7	26.9
Fall	4	15.4
Winter	7	26.9
	<u>26</u>	<u>100.0</u>

*Sex.*—There were 14 males and 12 females in the group studied. This observation may be used as an argument against the relationship of gall-bladder disease, since cholecystitis is much more common in females than in males in the proportion of 3 to 1. In 301 cases of acute cholecystitis operated upon here during the same period, there were 89 males and 212 females.

*Race.*—The colored race had only 1 representative.

*Nationality.*—There were 20 Americans, 2 Poles, 1 Italian, 1 Austrian, 1 Englishman, and 1 Canadian.

TABLE II  
ACUTE PANCREATITIS  
AGE

DECADE	AGE	NO. OF PATIENTS	PERCENTAGE
1	0-9	0	0.0
2	10-19	1	3.8
3	20-29	5	19.3
4	30-39	3	11.5
5	40-49	9	34.6
6	50-59	5	19.3
7	60-69	2	7.7
8	70-79	1	3.8
		<u>26</u>	<u>100.0</u>

## ACUTE PANCREATITIS

### A REPORT OF 26 CASES

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ACUTE pancreatitis has been described as being one of the most dramatic of all diseases. It has been placed in the same category as ruptured ectopic pregnancy, since, in both, the classical description is one of profound shock. This impression in the latter instance has been changing because now most patients with ectopic pregnancy are operated upon before the lesion ruptures. In pancreatitis, however, many physicians are still reluctant to make the diagnosis in the absence of shock and cyanosis. An analysis of the cases here presented demonstrates that such findings are quite unusual. It was the relative mildness of symptoms and findings in severe cases in contrast to the classical description that aroused interest and prompted a study of our case records. We have noted that increased interest in the subject has brought about improved results in both the diagnosis and treatment of our own cases; for example, the three cases seen after this work was started were correctly diagnosed preoperatively.

The study covers twenty-six patients with acute pancreatitis operated upon at the Henry Ford Hospital. Cases not coming to operation and those definitely secondary to a perforating peptic ulcer are not included.

*Pathogenesis.*—The experimental work on acute pancreatitis is enormous in volume. The most comprehensive contributions in recent years are those of Wangensteen, in 1931, and of Dragstedt, in 1934. The work of the former was confined largely to pathogenesis, while the latter considered the cause of death as well. These phases of the subject have been the chief points of interest for many years.

Without rehashing the great bulk of material which is readily available, it may logically be stated that no one factor can be considered the etiological agent in all cases. Bile must still be accepted as the most important factor. Dragstedt concluded that 60 per cent could be explained on the old common channel theory, 10 per cent of these being caused by stone in the ampulla and the remainder by spasm or edema of the sphincter of Oddi as suggested by Archibald. Because of the impossibility of demonstrating a common channel in certain proved cases of pancreatitis, the bile factor has been severely censured and many fantastic theories promulgated. However, it must be accepted as the

all three of these unusual locations the pain was severe. Free blood in the peritoneal cavity, pooled in the right lower quadrant, may account for the location in the last instance, but does not give any reason for the absence of upper abdominal pain. No explanation is apparent in the two instances with localization at the umbilicus.

While pain was noted in all cases, nausea was absent in only 1 and actual vomiting occurred in 24. In 1 the vomitus was continually streaked with blood and in another in which obstipation and distention were marked, the vomitus was considered to be fecal in nature. No special comment could be made in regard to the vomiting in the remainder, except that it was repeated. Beyond pain, nausea, and vomiting, no other persistent symptoms were noted. An analysis of the isolated occurrence of interesting symptoms, as noted in Table IV, indicates the relative lack of pathognomonic symptoms. The story as given by the patient is not of any great help in arriving at a diagnosis in practically 100 per cent of the cases considered. The onset of steady pain, reaching its acme early, is the possible exception.

TABLE IV  
ACUTE PANCREATITIS  
Rarer Symptoms

SYMPTOM	NO. OF PATIENTS	PERCENTAGE
Pain in right shoulder	2	7.7
Pain in left shoulder	1	3.8
Pain in back	1	3.8
Chills and fever	2	7.7
No bowel movement for 2 days	1	3.8
Diarrhea	2	7.7
Abdominal distention of notable degree	4	15.4
Cold and clammy sensation	1	3.8
Cold sweats	1	3.8
Pregnancy (6 months' duration)	1	3.8
Puerperal state (3 days)	1	3.8

#### CLINICAL FEATURES

A survey of the findings on physical examination is somewhat more encouraging, since the objective symptoms demonstrate a tendency to uniformity and so provide clues of diagnostic value.

*Temperature.*—Table V indicates the temperature reading before operation. A subnormal temperature was recorded in 19.3 per cent of the patients and in 53.9 per cent the reading was not above 100° F. Elevation above 102° F. was noted in only 7.7 per cent. The inference is that infection plays a minor role in the etiology of acute pancreatitis.

*Pulse Rate.*—The pulse rate of the patient with acute pancreatitis, as recorded in Table VI, may be taken as an index of the degree of involvement of the pancreas. The pulse rate is surprisingly low. In a total of 38.5 per cent of the patients the rate was under 100 and in only

*Age.*—Acute pancreatitis may occur at any age. Its association with acute infection in childhood, especially mumps, has been stressed by Farman. Table II shows that 2 patients in this small series were under 20 years of age and that 3 of them were over 60 years old. More than one-third of the patients were between the ages of 40 and 49 and over one-half of them between the ages of 40 and 60. This finding is in support of the theory of relationship to gall-bladder disease, since this period is the gall-bladder age.

*Weight.*—It has been stated that patients with acute pancreatitis are usually obese. Table III indicates that, while slightly more than one-third of the patients whose avoirdupois was recorded preoperatively weighed more than 175 pounds, exactly one-half of them weighed less than 150 pounds.

TABLE III  
ACUTE PANCREATITIS,  
WEIGHT

WEIGHT IN LB.	NO. OF PATIENTS	PERCENTAGE
100-125	1	6.3
126-150	7	43.7
151-175	2	12.5
175-200 plus	6	37.5
Total as recorded	16	100.0
Unrecorded	10	
Total patients	26	

#### HISTORY

*Previous Gastrointestinal History.*—Only 10 of the patients, or 38.5 per cent of the series, gave a history that was negative for gastrointestinal symptoms. All of the remaining 16 patients had complained of symptoms which had led their medical adviser to suspect gall-bladder disease, but a positive diagnosis by biliary drainage or cholecystogram study had been made on only 3 patients. A history of an attack similar to the present one was obtained from 14 patients, or 53.8 per cent of the series. Seven of the patients had been jaundiced previously; 5 had suffered from bloating; 2, from upper abdominal distress after meals; 2, from fat intolerance; 2, from hives; and 2, from constant pain in the gall-bladder region. One patient complained of persistent vague digestive disturbance; 1, of hunger pain; and 1 of the group had had an appendectomy for a gangrenous appendix four months previously.

*Subjective Symptoms.*—The history commonly elicited was very similar to that of any other acute intra-abdominal catastrophe. Twenty-three of the patients had severe pain as the outstanding symptom, while in only 3 instances, or 11.5 per cent, was the pain classified as moderate. In 23 patients the pain was in the epigastrium; 2, at the umbilicus; and in 1 the only pain complained of was in the right lower quadrant. In

as epigastric was observed 17 times, or in 65.5 per cent of the cases. Tenderness was confined to the left upper quadrant once and, because of the subacute nature of the process and the presence of a palpable mass, a diagnosis of pancreatic cyst was made. In the remaining patient with tenderness restricted to the lower right quadrant, a diagnosis of acute appendicitis was made and the error was not apparent until free blood exuded as the peritoneum was opened via a McBurney incision. One patient in the group flatly denied any tenderness, but at operation there was found marked involvement of the pancreas with a patent foramen of Winslow and a large amount of free blood in the peritoneal cavity. She made a remarkably rapid recovery.

*Spasms.*—Muscle spasm in any acute intra-abdominal lesion varies with the duration and progress of the disease, so these findings depend largely upon the time after onset that the examination is made.

The extension of muscle spasm from the right hypochondrium to involve the epigastrium and left upper quadrant was noted 12 times, or in 46.3 per cent of the cases. Three of these were described as board-like. Only 5 times was the muscle spasm limited to the right upper quadrant, while in 2 cases it was limited to the left hypochondrium. The 1 case in which other findings were limited to the right lower quadrant also had muscle spasms in this area. In 1 case only was the midepigastrium the sole site of muscle spasm. Five times the examiner reported muscle spasm as entirely absent. All of these, however, had definite tenderness and elevated white counts. It is of special interest that the first time Cullen's sign was observed in a case of pancreatitis in this clinic, muscle spasm was entirely absent. The process in this case was of the fulminating type and the patient expired thirty-six hours postoperatively.

*Shock.*—Apparent shock was commented on in the records of 4 cases. An analysis of these records for true evidence of shock revealed it was present in only 2 instances if the pulse, temperature, and blood pressure changes are the criteria. Koster and Kasman report shock 7 times in 22 cases with a systolic blood pressure below 90 in 3 of them. Our somewhat larger series shows only one instance of a systolic pressure below 100.

*Palpable Mass.*—A definitely palpable mass was found 4 times, an incidence of 15.4 per cent. In all of these the process was still definitely acute.

*Cullen's Sign.*—Cullen's sign, the value of which has been reported in a previous communication, was noted 3 times, for an incidence of 11.5 per cent.

*Cyanosis.*—Cyanosis was observed and recorded only twice. A note as to its absence was found 6 times and in the remainder no mention



## SURGERY

TABLE V  
ACUTE PANCREATITIS  
TEMPERATURE

F. READING	NO. OF PATIENTS	PERCENTAGE
96.0-98.6	5	19.3
98.8-100	9	34.6
100.2-101	7	26.9
101.2-102	3	11.5
102.2-103	0	0.0
103.2-104	2	7.7
	<u>26</u>	<u>100.0</u>

23.1 per cent was it over 120. This finding is at variance with the older concepts of the disease, in which shock was stated to be an outstanding symptom.

TABLE VI  
ACUTE PANCREATITIS  
PULSE RATE

RATE	NO. OF PATIENTS	PERCENTAGE
60- 70	2	7.7
70- 80	1	3.8
80- 90	2	7.7
90-100	5	19.2
100-110	6	23.1
110-120	4	15.4
120 plus	6	23.1
	<u>26</u>	<u>100.0</u>

*Blood Pressure.*—The blood pressure findings did not vary remarkably from normal levels; in fact, the most noteworthy feature is the relatively high level when so much of the literature stresses the state of shock in which the patients are said to be found. The range is demonstrated in Table VII.

TABLE VII  
ACUTE PANCREATITIS  
BLOOD PRESSURE READING

SYSTOLIC IN MM. HG.	NO. OF PATIENTS	PERCENTAGE
90-100	1	3.8
100-110	1	3.8
110-120	5	19.3
120-130	6	23.1
130-150	8	30.8
150-200	2	7.7
Unrecorded	3	11.5
	<u>26</u>	<u>100.0</u>

*Objective Symptoms.*—Tenderness was confined to the right hypochondrium in only 6 instances, or 23.1 per cent; while in a series of 301 cases of acute cholecystitis, such a localization was apparent 280 times, or 93 per cent. A more diffuse tenderness which could be localized only

Positive tests for bile in the urine were obtained only 4 times, an incidence of 15.4 per cent.

*Icterus Index.*—Only 4 readings of the icterus index were recorded, none of which was particularly high. They varied from 10.0 to 14.0 with an average of 12.2.

*Blood Sugar.*—Observations of the blood sugar were equally disappointing. Only 8 preoperative recordings were found, 3 of which were elevated, varying from 128 to 147 mg. per cent.

*Blood Chloride.*—Blood chloride determination was done only once. In this case vomiting was a very pronounced feature and the chloride level was 380 mg. per cent. Experimentally Dragstedt found that the disease had little effect on the blood chloride level.

*Nonprotein Nitrogen.*—Five nonprotein nitrogen determinations were all in the upper limits of normal.

*Blood Diastase.*—Blood diastase was not determined in any of the earlier cases. In most of the later ones it was done only postoperatively and the results were not particularly abnormal. In 1 case low readings of 6 to 12 units were consistently found. Marked liver damage was thought to account for this. Another frank case of acute hemorrhagic pancreatitis gave several blood diastase readings of 12 to 14 units.

#### PREOPERATIVE DIAGNOSIS

The majority of patients with acute pancreatitis present clinical features which lead the observer to suspect disease of the biliary tract. On admission to hospital the first examiner recorded his early impression of the condition. Cholecystitis and cholelithiasis headed the list of possibilities in 16 of the 26 cases, or 61.5 per cent of the total. Perforated ulcer was considered on 7 occasions and acute intestinal obstruction in 4 instances. Acute appendicitis and acute diverticulitis were both mentioned twice, while tabetic crisis, angina pectoris, general peritonitis, subphrenic abscess, ureteral calculus, and mesenteric cyst each entered the diagnostic field once. Acute pancreatitis was mentioned as a possibility 10 times.

TABLE X  
ACUTE PANCREATITIS  
PREOPERATIVE DIAGNOSIS

DIAGNOSIS	NO. OF PATIENTS	PERCENTAGE
Acute pancreatitis	8	30.8
Acute cholecystitis	8	30.8
Perforated peptic ulcer	6	23.2
Diverticulitis	1	3.8
Mesenteric cyst	1	3.8
Appendicitis	1	3.8
Intestinal obstruction	1	3.8
	<u>26</u>	<u>100.0</u>

of it was made. The rate of respiration recorded in Table VIII coincides with such a lack of cyanosis; this is in definite contrast to the classical descriptions.

TABLE VIII  
ACUTE PANCREATITIS  
RESPIRATORY RATE

RATE PER MIN.	NO. OF PATIENTS	PERCENTAGE
16-24	16	61.6 (normal)
25-32	7	26.9
33-40	3	11.5
	<u>26</u>	<u>100.0</u>

*Jaundice.*—Jaundice was observed and noted in about one-fourth of the cases; namely, 6 times, or 23.1 per cent. This is in accord with the 4 observations of jaundice in the 22 cases reported by Koster and Kasman.

*Distention.*—Distention was recorded as marked in only 2 cases.

#### LABORATORY FINDINGS

*Leucocytosis.*—The most consistent laboratory finding was an elevated white blood count. The variation, however, was extreme, ranging from 8,550 in a case with marked hemorrhage into the transverse mesocolon and a large amount of free blood in the peritoneal cavity to 45,000 in another case with free blood and fat necrosis. Both patients recovered after long hospitalization.

The variation of the white count is demonstrated in Table IX. The largest number falls in the 20,000 to 30,000 bracket and the average count was found to be 21,000, which is somewhat higher than usually found in the reported cases available for study.

TABLE IX  
ACUTE PANCREATITIS  
LEUCOCYTOSIS

WBC PER CU. MM.	NO. OF PATIENTS	PERCENTAGE
8,000-10,000	1	3.8
10,000-12,000	1	3.8
12,000-15,000	4	15.4
15,000-20,000	8	30.8
20,000-30,000	9	34.7
30,000-45,000	3	11.5
	<u>26</u>	<u>100.0</u>

The polymorphonuclear count was recorded 24 times and varied from 83 per cent to 98 per cent. The average count was 88.6 per cent.

*Urinalysis.*—Urinalysis showed only one consistent feature, a positive test for albumin in 16 cases, an incidence of 61.6 per cent.

Reducing substances were noted only 4 times.

*Culture of Abdominal Fluid.*—Cultures of the abdominal fluid found at operation were made in only 10 instances and of these 4 were positive and 6 were negative. The organisms recorded were *Streptococcus viridans*, staphylococcus, gram-positive cocci, and nonhemolytic streptococci.

*Fat Necrosis.*—The liberation and activation of lipase, the fat-splitting ferment of the pancreas, is of frequent occurrence in acute pancreatitis. Certain isolated small areas of fat in the omentum and mesentery are affected. The activated ferment splits fat into fatty acids and glycerin. The latter is absorbed and circulating calcium unites with the fatty acids to form soaps. These areas appear as small yellowish plaques in the omentum and mesentery. Fat necrosis is so characteristic of the disease that a confident diagnosis of acute pancreatitis can be made in its presence; in fact, these areas often provide the first clue to the diagnosis. Fat necrosis was observed in 16, or 61.5 per cent, of our cases. No satisfactory explanation has been submitted as to why necrosis is present in some cases and absent in others or why isolated and not contiguous areas of fat are involved.

*Involvement of the Mesocolon.*—The potential space existing between the leaves of the mesocolon is continuous with the retroperitoneal space in which the pancreas lies. In view of this anatomic arrangement the infrequency of involvement of the mesocolon in acute pancreatitis is remarkable. A collection of fluid in the mesocolon was found in only 2, or 7.7 per cent, of our patients, and fat necrosis was observed in only 6, or 23.1 per cent, of the cases.

*Approach to the Pancreas.*—Although the pancreas is an entirely retroperitoneal organ, it may be exposed anteriorly after gaining access to the lesser peritoneal cavity. There are four avenues of approach to this space: (1) through the gastrohepatic omentum, (2) through the gastrocolic omentum, (3) through the transverse mesocolon, and (4) through the foramen of Winslow. The last named route is not often utilized because of its relatively small size and because in acute pancreatitis it is often obliterated by edema or by filmy adhesions. The lesser peritoneal cavity is seldom entered through the transverse mesocolon, because, in the first place, it entails elevating the greater omentum and the transverse mesocolon into the operative field and also because of a hesitancy on the part of the surgeon to adopt any maneuver that might endanger the middle colic artery. The most direct access to the lesser peritoneal cavity and body of the pancreas, with a right rectus or midline incision, is obtained by going through the gastrohepatic omentum, above the lesser curvature of the stomach. However, an equally satisfactory exposure is effected by going through the gastrocolic omentum below the greater curvature of the stomach. The latter route had the preference in our cases as it was chosen twice as many times as the former.

Table X summarizes the final preoperative diagnoses. A definite diagnosis of acute pancreatitis was made in 8 cases, or 30.8 per cent of the cases. In 1 patient the diagnosis was easy because he had been operated upon before for the same condition. The diagnosis in 3 patients was based on the presence of a bluish discoloration around the umbilicus, the so-called Cullen's sign. In our experience the presence of an upper abdominal mass and a positive Cullen's sign as was found in 2 of our cases provides the only definite diagnostic criteria, for, of the 8 positive diagnoses, only 2 were made without one or the other of these clues.

*Anesthesia.*—The bearing on mortality of the various anesthetics used is set forth in Table XI without establishing any point of significance. The effect of the anesthetic agent on the gravely ill patient merits more serious consideration than it usually receives. The relative harmlessness of local as compared with general or spinal anesthesia should not be overlooked when dealing with this and other conditions requiring surgical intervention in the poor risk patient.

TABLE XI  
ACUTE PANCREATITIS  
ANESTHESIA

AGENT	NO. OF PATIENTS	PERCENTAGE	NO. OF DEATHS	MORTALITY PERCENTAGE
Ethylene and ether	18	69.4	7	41.1
Ether alone	3	11.5	3	100.0
Spinal	4	15.4	2	50.0
Local	1	3.7	0	0.0
	<u>26</u>	<u>100.0</u>	<u>12</u>	<u>46.1</u>

*Incisions.*—The abdominal cavity was opened through a right rectus incision in 17 instances and on 3 occasions a left rectus incision was used. A high midline incision through the linea alba has much to commend it, though it was employed in only 6 of our cases. This latter incision has the great advantage of not opening into any of the fascial compartments so that, if infection or tissue digestion ensues, there is less destruction of those important structures which maintain the integrity of the abdominal wall. This precaution will lessen the incidence of postoperative ventral hernia and will make possible a more effective repair when hernia does develop.

#### OPERATIVE FINDINGS

*Abdominal Fluid.*—In 12 patients, or almost one-half of the cases, there was no excess fluid found in the peritoneal cavity. In the remaining 14 patients an abundance of bloodstained fluid was observed. In 12 instances the fluid was described as being stained with fresh blood and in 2 occasions with altered or old blood.

this possible probably occurs in about 60 per cent of cases, as shown by reports fluctuating from 3.5 per cent to 89 per cent.

The question which naturally arises is why is pancreatitis so infrequent if it is caused by spread of infection from the gall bladder either through the lymphatics or by way of the biliary passages? There were 1,716 cholecystectomies performed at the Henry Ford Hospital during the same period the 26 cases of acute pancreatitis of this series were observed. This gives a ratio of 66 to 1, a figure almost identical with that given by Abel who found 30 operations for acute pancreatitis and about 2,000 operations in the biliary tract. Furthermore, if the gall-bladder origin hypothesis is the correct one, acute pancreatitis should be more commonly associated with acute than with chronic cholecystitis and yet Table XIII shows the reverse to be true, for the gall bladder was acutely inflamed in only 15.4 per cent of the cases. Finally, how are we to explain these cases of acute pancreatitis in which the gall bladder shows no evidence of disease? The clinical course of the disease in fulminating cases suggests an overwhelming infection. It may be that a generalized infection becomes localized in the pancreas in the same manner that the lungs bear the brunt of a pneumonic infection.

*Operation Performed.*—Table XIV summarizes the operations performed on the patients of this series. The best results were obtained in those cases where the operation simply consisted of drainage of the lesser peritoneal cavity. Eleven patients were treated in this manner with 5 deaths, a mortality rate of 27.7 per cent. When cholecystostomy was added, as it was in 13 cases, there were 8 deaths, a mortality rate of 61.8 per cent; and death occurred in 2 of the 4 patients in whom the gall bladder was removed and the common bile duct drained, a mortality of 50 per cent. The finding of a mortality rate of 46.1 per cent, even in such a serious disease as acute pancreatitis, suggests that the method of treatment currently in vogue should be reviewed critically. It has been the procedure in this clinic to operate upon all cases of acute pancreatitis as soon as they are diagnosed or suspected. The fluid balance, of course, is restored and blood transfusions are given to forestall or combat shock. All the patients in the series except the last 3 were treated in this manner.

TABLE XIV  
ACUTE PANCREATITIS  
OPERATION PERFORMED

OPERATION	NO. OF PATIENTS	PERCENTAGE	NO. OF DEATHS	MORTALITY
Drainage alone	11	42.3	3	27.7
Drainage plus cholecystectomy	2	7.7	1	50.0
Drainage plus cholecystostomy	13	50.0	8	61.8
	<u>26</u>	<u>100.0</u>	<u>12</u>	<u>46.1</u>

*Region of Pancreas Involved.*—Table XII shows that the whole of the pancreas was involved in 19, or 73.1 per cent, of the cases and that the process was limited to the head in 5, or 19.2 per cent, and to the tail in 2, or 7.7 per cent.

TABLE XII  
ACUTE PANCREATITIS  
REGION OF PANCREAS INVOLVED

REGION	NO. OF PATIENTS	PERCENTAGE
Whole pancreas	19	73.1
Head only	5	19.2
Tail	2	7.7
	26	100.0

*Gall-Bladder Involvement.*—Table XIII illustrates the frequency with which gall-bladder disease and acute pancreatitis coexist. The finding of 73.1 per cent of our patients with pathologic gall bladders serves to emphasize the relationship which has been stressed by all authors on the subject. The gall bladder and pancreas have much in common; their ducts normally enter into the duodenum together, though the exact relationship varies; their blood supply arises from the same source; and their lymphatic vessels have a rich anastomosis. Of the 3 possible routes for spread of infection from the gall bladder to the pancreas, the lymphatic route appears to be the most feasible. Some support of this theory is given by a consideration of the frequency with which mild degrees of chronic pancreatitis are found in cases of cholecystitis and cholangitis.

TABLE XIII  
ACUTE PANCREATITIS  
GALL-BLADDER INVOLVEMENT

DEGREE	NO. OF PATIENTS	PERCENTAGE
Chronic cholecystitis	15	57.7
Acute cholecystitis	4	15.4
Gall bladder negative	7	26.9
	26	100.0

Biliary calculi were present in the gall bladder in 15, or 50 per cent, of the 19 cases in which the gall bladder was obviously diseased, but were found only twice in the common duct at operation. However, in one patient who expired, autopsy revealed a single small stone plugging the ampulla of Vater. No doubt there were other examples of common duct calculi in the series, for, even under the most favorable conditions, small stones are frequently unrecognized and all the more so when exploration must be hurried because of the condition of the patient. Gallstones, of course, can be a factor in acute pancreatitis only under circumstances in which obturation of the ampulla of Vater permits reflux of bile into the pancreatic ducts. The anatomic variation making

## MORTALITY

The duration of the disease prior to operation has received a great deal of attention in recent years. The growing conception is that, if operation is delayed beyond the period of early insult, the prognosis can be improved. Recent authors have gone so far as to recommend absolutely conservative treatment, and, finally, after complete convalescence, elective biliary tract surgery.

In the present series, 22 patients were operated upon during the first week of the disease. The following facts are of interest in their relation to mortality. Seven of these patients were operated upon on the second day. Of these 7, 3 died, 2 in less than 24 hours and the third in 72 hours. This gives a mortality following second-day operations of 42.8 per cent in contrast to a 46.2 per cent mortality in the entire group.

Those operated on the third day did not fare so well in that all three expired in short order, 2 early in the second postoperative day, and the other did not leave the operating room.

The three patients operated upon during the first 24 hours of the disease recovered, while one operated upon on the nineteenth day in a moribund condition lived only 8 hours.

The early days of the disease, after the first 24 hours, appear to be the most dangerous for operation. It is not until the eighth day is reached that a definite drop in mortality is noted.

The most outstanding feature in regard to mortality is the short span of life postoperatively. Twelve deaths occurred in the series, 8 of them within the first two days following operation, an average duration of life of only 21 hours. Two more deaths occurred on the third postoperative day. The question worthy of consideration is whether or not any of

TABLE XVI  
ACUTE PANCREATITIS  
RELATION OF MORTALITY TO TIME OF OPERATION

DAY OF DISEASE OPERATED UPON	NO. OF OPERATIONS	NO. OF DEATHS	DURATION OF LIFE	MORTALITY RATE
1	3	0	--	--
2	7	3	16 hr.	--
			72 hr.	42.8
			7 days	
3	3	3	20 hr.	100.0
4	3	2	24 hr.	66.6
5	1	0	--	--
6	3	2	10 hr.	--
			3½ days	66.6
7	2	1	17 days	50.0
8	1	0	--	--
13	1	0	--	--
18	1	0	--	--
19	1	1	8 hr.	100.0



It is interesting to conjecture why early authors on the subject felt that it was so necessary to evacuate the products of pancreatic necrosis. Their teaching has been followed by most surgeons in spite of the work of Whipple, who, as long ago as 1913, demonstrated that the peritoneal exudate in acute hemorrhagic pancreatitis was innocuous when injected into the veins and peritoneal cavities of animals. The modern trend is to treat acute pancreatitis conservatively and to operate only when a definite mass appears. The results of drainage of these pseudocysts and abscesses are extremely good and the mortality is low. The proponents of the conservative treatment feel that immediate operation does not benefit the fulminating cases and that the added insult of the anesthetic and the operative trauma may turn the tide against the patient. Their contention receives further support from the conclusions of practically all observers that the outcome of a case depends on the degree of involvement of the pancreas and that this is often determined by the time the patient is seen by the surgeon. Decompression of the biliary system, in our cases at least, did not fulfill the theoretic expectations since the mortality rate in those cases in which cholecystostomy was performed was almost double that of simple drainage of the lesser peritoneal cavity. However, it is conceivable that in the early edematous stage of acute pancreatitis decompression of the biliary system might be of value because there are cases on record in which only edema of the pancreas was found at operation, and yet the patient went on to die of a fulminating pancreatitis. The great drawback of the expectant attitude is in the difficulty of making an accurate preoperative diagnosis. Directly as a result of this study we have treated conservatively our recent cases of acute pancreatitis, including the last three of this series. All of the patients recovered following drainage of abscesses or pseudocysts.

*Duration of Operation.*—The duration of the operation apparently had little to do with the prognosis, except those lasting an hour and fifteen minutes carried by far the greatest mortality as a consideration of Table XV will indicate.

TABLE XV  
ACUTE PANCREATITIS  
DURATION OF OPERATION

DURATION OF OPERATION IN HR.	NO. OF OPERATIONS	NO. OF DEATHS	MORTALITY PERCENTAGE
$\frac{3}{4}$	4	2	50.0
1	9	4	44.4
$1\frac{1}{4}$	7	6	85.7
$1\frac{1}{2}$	4	0	0.0
$1\frac{3}{4}$	1	0	0.0
2	1	0	0.0
	<u>26</u>	<u>12</u>	<u>46.1</u>

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these patients could have tolerated the insult of the pancreatitis had they not been brought to bear the shock of an operation. Many years ago Whipple demonstrated that dogs with experimental pancreatitis had a better chance for recovery if the abdomen was not opened.

Table XVI gives a composite view of the mortality rate and duration of life in relation to the day of disease on which operation was performed.

*Hospital Stay.*—The period of hospitalization varied from 16 to 96 days. Of the 14 patients who recovered, 9 had an average hospital stay of 19½ days, which is not much longer than the anticipated time for other upper abdominal surgery. In the remaining 5 cases the average period of hospitalization was 60 days.

*Recurrences.*—Five of the 14 patients who recovered were readmitted with findings which were taken as indication of a recurrence of pancreatitis. Four of them were followed conservatively. The fifth was operated upon and he expired. Necropsy revealed an acute pancreatitis with widespread necrosis.

#### SUMMARY AND CONCLUSIONS

1. An analysis of 26 cases operated upon for acute pancreatitis at the Henry Ford Hospital is presented.

2. Noteworthy features of the cases were the general mildness of the symptoms and the absence of shock.

3. A correct preoperative diagnosis was made in 30.8 per cent of the cases.

4. All but 3 cases were treated by immediate operation.

5. The mortality rate was 46.1 per cent.

6. With simple drainage of the lesser peritoneal cavity, the mortality was only 27.7 per cent, but, when cholecystostomy was added, the mortality rose to 61.8 per cent.

7. The short duration of life postoperatively in the fatal cases suggests that operation precipitated the fatal outcome.

8. A direct result of this review has been a tendency toward delayed operation.

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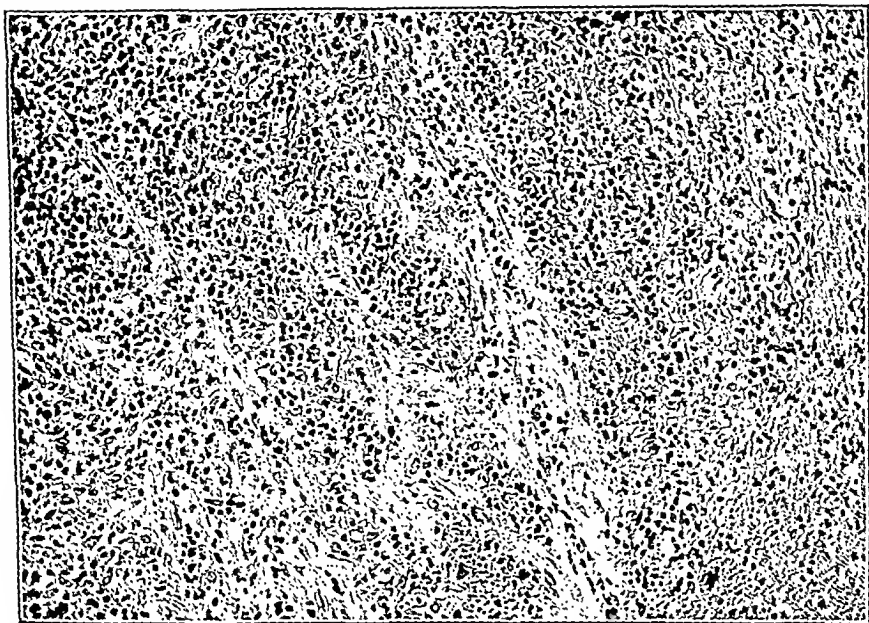


Fig. 1.—Wall of appendix, showing destruction of normal architecture, diffuse infiltration with eosinophilic and neutrophilic leucocytes, and deposits of fibrin (low power,  $\times 200$ ).

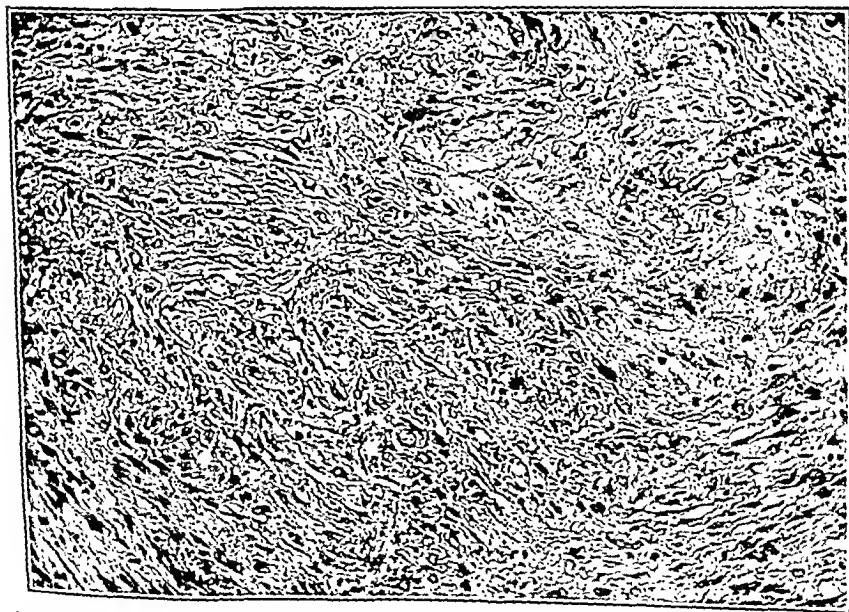


Fig. 2.—Periappendiceal mass. Granulation tissue with large number of fibroblasts and capillaries; infiltration with leucocytes, chiefly neutrophils (low power,  $\times 200$ ).

## ACUTE SUPPURATIVE APPENDICITIS COMPLICATING SEVERE UNTREATED THYROTOXICOSIS

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THE occurrence of acute abdominal crises in such intoxications and metabolic disturbances as plumbism and diabetes mellitus, although infrequent, is quite well known. Of greater rarity is the occurrence of acute abdominal pain in thyrotoxicosis. A few cases have been reported by Stern,<sup>1</sup> Kraus,<sup>2</sup> Horsley and Rosebro,<sup>3</sup> and Desbouis.<sup>4</sup> More recently Robertson and his associates<sup>5</sup> have dealt with this problem. They reported three cases of "hyperthyroidism masked by symptoms of acute abdominal catastrophe," and in one case the abdominal symptoms so closely mimicked acute appendicitis as to cause a surgical consultant to remove the appendix, which proved to be normal. On the other hand, failure to recognize a true acute intra-abdominal lesion requiring immediate surgical intervention may be disastrous. The difficulties in differential diagnosis are obvious and require no further comment.

In a consecutive series of over 2,000 patients requiring thyroidectomy for thyrotoxicosis, Richter<sup>6</sup> has had occasion but twice to perform laparotomy for acute intra-abdominal disease. Interestingly enough, in both patients the operation was undertaken for acute suppurative cholecystitis. In these two instances the patients were under treatment for thyrotoxicosis (receiving Lugol's solution in adequate dosage) which minimized the danger of postoperative reaction. In the case to be presented, a somewhat different problem was encountered. Here we had to deal with a patient who had an acute suppurative intra-abdominal lesion, but who also presented most marked symptoms of high grade hyperthyroidism for which she had never been treated. One needs but to recall the high mortality and morbidity associated with operations on the thyroid gland (for thyrotoxicosis) in the preiodine era, as well as the occurrence of thyroid crisis following apparently trivial surgical procedures (as incision of a furuncle or infection of a varicose vein<sup>7</sup>) to understand the surgical problem encountered in this patient. The salient facts are herewith presented.

### REPORT OF CASE

I. B., a 23-year-old white girl, first came under observation in October, 1934, complaining of palpitation, heat intolerance, and nervousness. She had been perfectly well until that time. The past history was without significance; the menses began at 13 years of age, and were of the regular 30-day type, duration 5 days.

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Abdominal examination disclosed diffuse tenderness, most marked in the right lower quadrant over the appendiceal area, right rectus rigidity, marked rebound tenderness, and a positive Rovsing sign. On rectal bimanual examination (the hymen was intact), there was tenderness high up on the right side. The leucocyte count was 18,300, with 78 per cent polynuclears; there were no urinary abnormalities. The diagnosis made was acute suppurative appendicitis and severe hyperthyroidism, and the patient was immediately hospitalized.

Realizing the grave danger of laparotomy in the presence of severe thyrotoxicosis, it was thought best to defer operation for some eight to ten hours, during which time we could institute measures to lessen the risk of crisis. Accordingly, she received 4,500 c.c. of normal saline solution with dextrose (5 per cent) intravenously, and sodium iodide, 75 gr. (5.0 gm.) by the same route in divided doses. Morphine sulfate was administered twice in quarter grain doses during this interval.

The pulse rate remained at 160 per minute, but the patient felt less nervous, irritable and restless.

*Operation and Clinical Course.*—Operation was performed on Aug. 6, 1937, some forty-eight hours following the onset of the abdominal pain. Under nitrous oxide-oxygen anesthesia with infiltration of the abdominal wall with 0.5 per cent novocain solution, the abdomen was opened through a muscle-splitting incision. A small amount of free turbid peritoneal fluid escaped and a large acutely inflamed mass was encountered, consisting of the appendix and an adherent tumor lying in a small pool of pus. The entire mass was quickly delivered and removed without inverting the appendical stump, and the abdomen closed without drainage. (The gross appearance of the removed tumefaction was that of an acutely inflamed appendix with a granuloma or carcinoid tumor.) During the operation the pulse rate varied from 160 to 180 per minute, and the systolic blood pressure readings fluctuated from 140 to 168, the diastolic level remaining at 80.

The immediate postoperative treatment consisted of continuation of the phlebotomy with saline solution and dextrose (5 per cent) and Lugol's solution equivalent to 120 minims during the first 24 hours, 60 minims daily for the next three days, and 45 minims daily thereafter. Morphine and phenobarbital were used liberally for sedation. The first five postoperative days were stormy; the temperature ranged from 101° F. to 104° F.; the pulse rate varied from 120 to 180 per minute and the patient was restless and extremely irritable, although as cooperative as circumstances permitted. The temperature gradually declined and the pulse rate diminished, the former reaching normal on the ninth postoperative day. Convalescence thereafter was smooth, being marred only by a mild wound infection which yielded readily to Dakinization. She was discharged on the twenty-first postoperative day, with the wound healed, and advised to return in three weeks for thyroidectomy. The basal metabolic rate on discharge was plus 26.

*Second Operation.*—The patient returned for thyroidectomy three weeks after discharge from the hospital, having been on Lugol's solution, 45 minims daily, during the interval. She had gained seven pounds and had improved remarkably. The preoperative basal rate was plus 15. Subtotal thyroidectomy was performed under nitrous oxide-oxygen anesthesia with infiltration of the skin and muscles with 0.5 per cent novocain solution. A large symmetrical hyperplastic gland was removed. Recovery was uneventful and she was discharged on the seventh postoperative day, with a basal metabolic rate of plus 10. She has remained well since discharge following the thyroidectomy.

*Pathologic Report.*—(Dr. I. Davidsohn.) Acute suppurative appendicitis and periappendicitis; granuloma; hyperplastic goiter.

The essential physical findings at this time consisted of slight, diffuse, symmetrical thyroid enlargement, pulse rate of 92 to 100, tremor of fingers and tongue, systolic blood pressure of 128, and diastolic pressure of 65. Two basal metabolic rate determinations at this time were plus 28 and plus 30. A diagnosis of toxic (diffuse) goiter was made and the patient was advised to have thyroidectomy after proper iodine preparation. This was refused and she was not seen again for over a year, when she again presented herself with the same, but more marked, symptoms. The palpitation was now more persistent; there was slight bilateral equal exophthalmos; weight loss of 12 pounds in the preceding 8 weeks had occurred; the skin was warm and moist, the pulse rate 110 to 120, systolic blood pressure 136 and diastolic pressure 60. The basal metabolic rate was plus 28. She again refused thyroidectomy. She was seen on two occasions in the next eighteen months, and attention was called to the definite progression of symptoms, but all efforts to persuade her to accede to surgical treatment were futile.



Fig. 3.—Hyperplasia of thyroid. Epithelial cells are high columnar. Many papillary projections are seen. Colloid is thin or absent. (Low power.  $\times 200$ .)

Such was the state of affairs when on the evening of Aug. 4, 1937, she was seized with severe generalized abdominal pain. She became nauseated, felt "feverish," but did not vomit. The pain became cramplike, and the next morning was most marked in the right lower abdominal quadrant. She vomited three times on the following day. There were no urinary disturbances, no diarrhea, and no symptoms referable to the respiratory tract. She was seen by us on Aug. 6, 1937, some forty hours following the onset of abdominal pain. Her appearance was that of a seriously sick patient. She was restless, irritable, and tremulous; the cheeks were flushed, and the skin, warm and moist. The temperature was  $103^{\circ}$  F. (rectally), the pulse rate 160, and the blood pressure 150/70. There was moderate bilateral equal exophthalmos, tremor of tongue, diffuse symmetrical enlargement of the thyroid, and tremor of the outstretched fingers. There were no cardiac abnormalities, save for the tachycardia and a soft systolic apical murmur which was not transmitted.

Abdominal examination disclosed diffuse tenderness, most marked in the right lower quadrant over the appendiceal area, right rectus rigidity, marked rebound tenderness, and a positive Rovsing sign. On rectal bimanual examination (the hymen was intact), there was tenderness high up on the right side. The leucocyte count was 18,300, with 78 per cent polymorphonuclears; there were no urinary abnormalities. The diagnosis made was acute suppurative appendicitis and severe hyperthyroidism, and the patient was immediately hospitalized.

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## SUMMARY

A case of acute suppurative appendicitis is reported, which occurred in the course of a severe untreated thyrotoxicosis. Appendectomy was successfully carried out following an eight-hour preparation with large doses of iodine intravenously, phlebotomy, and sedation with morphine. Thyroidectomy was performed later without incident.

Attention is directed to the rarity of acute abdominal pain occurring in thyrotoxicosis, the difficulty in differentiating the pain due to organic intra-abdominal disease requiring surgical intervention from the abdominal pain which may be due to the underlying intoxication, and the grave danger of operating upon thyrotoxic patients improperly prepared.

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## LEFT RETROMESOCOLIC HERNIA

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IN A PREVIOUS communication<sup>1</sup> I presented a case of right retromesocolic hernia. At that time there were on record forty-nine authentic cases of this kind of hernia. Since then two others have been added, one by Paul and Hill<sup>2</sup> and another by Baumeister and Hanchett.<sup>3</sup> Recently it was my good fortune to encounter a case of left retromesocolic hernia, a condition first described in detail by Treitz (1857) and since then called the hernia of Treitz. According to the figures given by Moynihan,<sup>4</sup> Andrews,<sup>5</sup> and Longacre,<sup>6</sup> left retromesocolic hernia seems to occur about three times more frequently than the right. In most of the recorded instances, as in that of Callander, Rusk, and Nemir,<sup>7</sup> and that of Emenhiser and Pankratz,<sup>8</sup> the hernial sac contained all of the jejunum and almost all of the ileum. In the case herein described, only a portion of the jejunum was enclosed in the hernial sac and the peritoneal and vascular relations were thus well enough preserved to illuminate the mechanism producing this condition.

### CASE REPORT

S. B., a 55-year-old colored man, was admitted to the Charity Hospital of Louisiana at New Orleans, Aug. 25, 1938, in a state of unconsciousness. According to a friend, he had been a heavy drinker for two years and on the day before admission he was found naked and unconscious, with short, stertorous breathing, and was bathed in sweat. His blood pressure was unobtainable; the pulse rate was 100 per minute; the respirations, 28; and the rectal temperature, 102° F. The cardiac impulse was not seen or felt, the heart tones were of poor quality, and the rate and rhythm were regular. Large, moist râles were heard over both lungs. The urine was bloody. Supportive treatment was of no avail. On the following day the patient's temperature rose to 104° F. and he died at 11:05 A.M., about fifteen hours after admission.

The necropsy (A-38-862) revealed bronchitis, bronchiolitis, and lobular pneumonia, an enlarged prostate, hypertrophy of the urinary bladder with diverticula and acute cystitis, slight cirrhosis of the liver, a small accessory spleen, and an intraperitoneal hernia. The latter was of particular interest.

The peritoneal cavity contained no excess fluid and its surfaces were smooth and glistening. No changes were noted in the disposition of the upper abdominal organs. Below the transverse mesocolon, on the left side of the vertebral column, there was a peritoneal pocket, 12 by 12 cm., with an oval opening to the right 8 by 7 cm. Near the free margin of the peritoneal fold bordering the opening ran the inferior mesenteric vein and the ascending branch of the left colic artery.

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The pocket, situated in the region of the duodenojejunal fossa, contained the left inframesocolic portion of the duodenum and about 90 cm. of jejunum. The loops of jejunum were easily removed, since they were practically empty and there were no adhesions between the loops or the pocket. The rest of the jejunum and the ileum was collapsed and empty. The appendix was in a medial position and 6 cm. long. The position of the cecum, colon, and rectum was as usual.

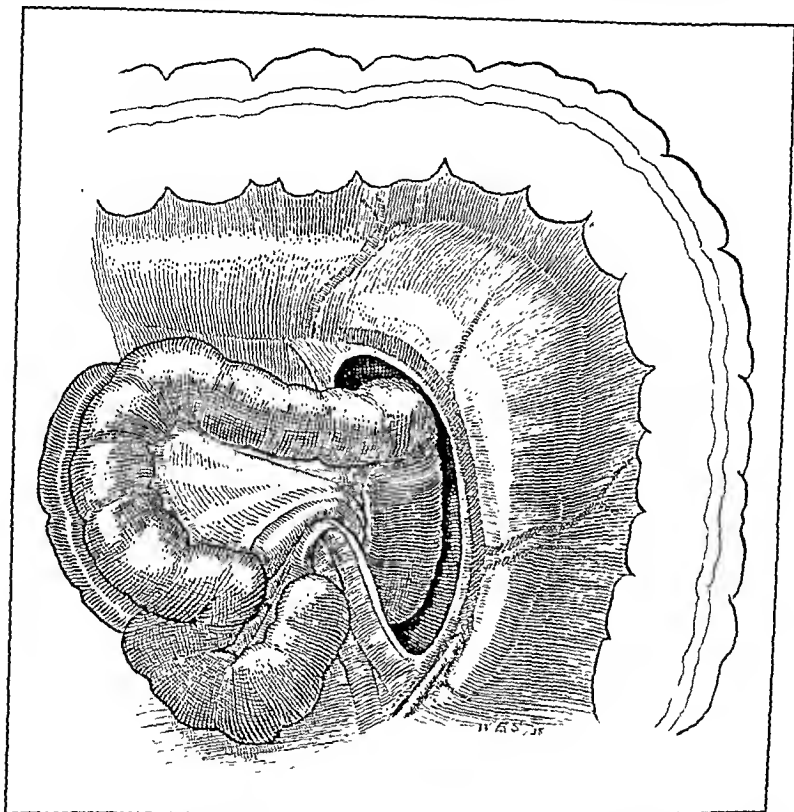


Fig. 1.—Below the transverse mesocolon, in the region of the duodenojejunal fossa, there is a peritoneal pocket which contains the left inframesocolic portion of the duodenum and from which 90 cm. of jejunum have been removed. The anterior wall of the pocket containing the inferior mesenteric vein and the left colic artery in their usual relation is a part of the descending mesocolon, hence the name *hernia retro-mesocolica sinistra*.

#### COMMENT

This hernia, like the type which occurs on the right side, is to be interpreted as a malposition of the part of the small intestine involved, rather than as a herniation into a preformed peritoneal sac. This malposition is due to a faulty orientation of the developing gut during that period of its rotation when the cecum migrates toward the right iliac fossa and the descending mesocolon becomes fused with the parietal peritoneum. The failure of the craniomedial half of the descending mesocolon to fuse with the parietal peritoneum leaves a pocket enclosing a part of the duodenum (the left inframesocolic portion) and some loops of the

proximal jejunum. This pocket, which forms the hernial sac, opens toward the right. Its anterior wall, which contains the inferior mesenteric vein and the left colic artery in their usual relation, is a part of the descending mesocolon, hence the name *hernia retromesocolica sinistra*.

#### SUMMARY

Malposition of a part of the small intestine in a peritoneal sac behind the descending mesocolon is described and interpreted as a left retromesocolic hernia. This type of hernia is about three times more frequent than that occurring on the right side.

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## HERNIA THROUGH THE BROAD LIGAMENT

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(From "The Clinic")

ONLY sixteen cases of true hernia into or through the broad ligament have been reported to date. All of these, save one, have been of the intestinal type. In this single case, reported by Masson and Atkinson, the hernial sac contained a Fallopian tube and ovary. The first authentic case of broad ligament hernia was that described by Quain in 1861. He performed an autopsy on a 36-year-old multipara who had died, without operation, following an incarceration of small intestine through an opening in the right broad ligament. There is a long hiatus in the literature until 1917, when Fagge reported two cases of intestinal hernia through the broad ligament. Since that time, the following additional cases have been reported: 1920, Barr (1), Richardson (1); 1924, Pidcock (1); 1926, Dunn (1); 1928, Dorman (1), Stimson (1); 1929, Pemberton and Sager (1), Janes (2); 1930, Coplan (1); 1931, Cooper (1); 1933, Masson and Atkinson (1); 1934, Hunt (1). Total cases to date, 16.

Of this number, only two have followed the Baldy-Webster operation for uterine suspension. These were the cases of Richardson and Pemberton and Sager. Straugulated hernias through the broad ligament were found in both of these patients at two years and ten days, respectively, following the uterine suspensions. Our first case, an account of which will follow, is the third case to be reported of broad ligament hernia following the Baldy-Webster uterine suspension.

The youngest case of the series was reported by Hunt. The patient was 25 years old and the hernia was incidentally discovered when she was being delivered of her third child by low cervical cesarean section. Undoubtedly as our attention is drawn to this condition more cases will be reported. The oldest in the series was Cooper's case, aged 70 years. The patients were almost exclusively multiparous, most of them having borne three or more children. Two were nulliparas, aged 49 and 30 years. The average age incidence for 15 of the 16 cases was 49 years; Dorman did not give the age of his patient. Of the total series of 16, 6 of the hernias occurred on the right, while 10 involved the left broad ligament. No case has yet been reported in which a hernia has been present on both sides simultaneously. Dunn's case, however, had a large window through the broad ligament opposite the site of the broad ligament hernia. The cecum and appendix were adherent to the edge of the

ring and it is quite conceivable that, had there been a mobile cecum, this could easily have passed through so large an aperture as was present in the right broad ligament.

#### ETIOLOGY

As usual we must consider predisposing and exciting causes. Developmental anomalies, such as pouches, fenestrations, or mere anatomic weakness in the intrinsic structure of the broad ligament must be mentioned. As a rule textbooks make but scant mention of the embryology of the broad ligaments, but Kostancecki has brought out the fact that, even in the adult normal broad ligament, a degree of weakness persists along the lines of fusion between the medial and lateral parts of the Wolffian mesentery and the phrenicomesonephric ligament. Given the predisposing congenital weakness of this structure plus the necessary force, a hernia may result by the wedging and dissecting action of the viscus which is being thrust in the direction of least resistance. In the series of 5 broad ligament hernias collected by Dunn, all of the hernias entered the openings from above and behind. As Dunn points out, this is the plane which the broad ligaments present to the intestines and which bears the brunt of intra-abdominal pressure. In Richardson's case and in our first case, both of which followed the Baldy-Webster uterine suspension, the gut passed through the hernial opening from before backward. In Pemberton and Sager's case, however, after the same type of operation, the gut passed through the hole in the reverse direction.

Multiparity and middle age with their relaxations of tissues are further important predisposing causes. The Baldy-Webster operation in which a hole is torn through the broad ligament on each side and through which the relaxed round ligament is pulled to be sutured to its fellow on the posterior surface of the uterus is a very important potential source of trouble. In Richardson's case the Baldy operation had been performed two years previously without suture of the openings through the broad ligaments as urged by the originators of the operation. He found three or four inches of gut strangulated in the opening in the right broad ligament. Pemberton and Sager report another such occurrence in a patient ten days after the Baldy-Webster operation. In this case both openings in the broad ligament had been closed according to the original technique. They also reported a second patient who was operated on for large uterine myomas. She had had a Baldy-Webster suspension operation twelve years previously. At hysterectomy the operators made the incidental findings of a large opening in each broad ligament where the tunnels had been placed for the round ligaments. The openings, however, contained no viscera. Hence, whether the openings through the broad ligaments are sutured according to the original technique or not, one cannot be entirely safe. It

would seem that, if the Baldy-Webster operation is ever performed, these openings should be firmly sutured with nonabsorbable material. The herniation may take place a few days or many years after the Baldy operation. Among the exciting causes of broad ligament hernia should be mentioned falls, straining at stool, or during childbirth, or any violence whereby a viscus could be thrust through an already weakened tissue. Not infrequently there is no tangible exciting cause. In the case of the larger openings it is quite conceivable that a loop of gut may be present in a hernial pouch or may even be thrust for a considerable distance through an aperture without detection until at some future date the crisis is precipitated and the true condition discovered. As Hunt has brought out, the broad ligament is divided into two triangular areas; the smaller portion is uppermost and is separated topographically from the lower and larger triangle by the ligamentum proprium ovarii. The hernias may pass through either of the triangles.

#### DIAGNOSIS

There are no infallible diagnostic criteria. Hernias through the broad ligament present the same variations and vagaries of symptomatology that are seen in other types of acute intestinal obstruction and are subject to the same delays in therapy. Any patient who has had a Baldy-Webster operation, no matter how many years previously, and who develops sudden acute obstructive symptoms referable to the intestinal tract may have a broad ligament hernia. Unfortunately tenderness in the cul-de-sac or in the region of the adnexa or the presence of a palpable tender mass in these areas is not of much help. It is quite possible to have a broad ligament hernia with no symptoms nor findings suggesting trouble within the pelvis.

#### TREATMENT AND PROGNOSIS

The treatment is operative and should be carried out immediately or temporarily deferred according to whether the patient's condition will permit or whether time must be taken to replace lost fluids and blood chlorides. The earlier the operation, the better the prognosis. Those who are operated upon too late will die, just as will those patients with acute ileus due to any other cause. In the series of 16 cases of hernia through the broad ligament, 15 were operated upon. Quain's case in 1861 was examined only at autopsy without having been operated on. Eleven recovered, 3 with stormy convalescences due to complications. Janes' second patient, who was suffering from auricular fibrillation at the time of operation, died seventeen hours after laparotomy. Stimson's case was hopelessly ill from a four-day bowel blockage and died shortly after the peritoneum was opened. Most of the cases received general anesthesia, but we favor the use of spinal anesthesia whenever possible for reasons which must be obvious without detailed argument.

In some cases the fenestrae or pouches in the broad ligament may be closed by suturing. At other times the offending area is removed by salpingo-oophorectomy. Again it may occasionally suffice to simply incise the roof of the tunnel through the broad ligament, as we did in our case, peritonizing the raw edges as they retract in order to eliminate re-formation of the aperture.

#### ADDITIONAL CASE REPORT

CASE 17.—Aged 42 years, Caucasian-Hawaiian, gravida iii, para ii. She was brought to our office in a state of collapse, Feb. 25, 1938, at noon. She had been teaching school as usual from early in the morning. Forty-five minutes before we saw her she was seized as she stood by an agonizing pain low in the left pelvis. She fainted and felt very weak when she regained consciousness. She was nauseated but did not vomit at the time. Generalized pallor was noted and the entire body was bathed in clammy sweat. Blood pressure was 120/68. Abdomen flabby with old healed striae gravidarum; no distention; no rigidity but generalized moderate degree of tenderness noted. Usual tinkling type of peristalsis heard throughout abdomen. On pelvic examination uterus approximately normal size but very hard with a smooth round walnut-sized knob palpable on its upper left anterior surface. No cul-de-sac or adnexal masses or tenderness was noted. Knee jerks slightly accentuated. Hemoglobin (Newcomer), 48 per cent; red blood count, 2,500,000. Urine normal except for a very faint trace of albumin. She was admitted at once by ambulance to Queen's Hospital where efforts were directed toward combating shock. It was felt that immediate laparotomy was inadvisable. She was given 500 c.c. of citrated whole blood intravenously shortly after her admission with noticeable improvement. In addition Hartmann's solution was given in liberal quantities intravenously. As she improved, a more coherent history was obtained from her. She had been in excellent health until after her children were born. These were born normally twenty and sixteen years previously. Following that she induced a miscarriage nine years ago at five and one-half months. Menstrual history: Onset at 12 years of age, irregular until marriage. Occasional slight dysmenorrhea. Sixteen years ago she had had a Baldy-Webster operation done for retroversion of the uterus. On Dec. 31, 1937, she consulted us regarding profuse vaginal bleeding recurring two or three times a month and lasting for as long as seven successive days. An irregular hard knobby uterus was clearly felt. Operation was advised, but this was declined. She received radium therapy elsewhere. The bleeding ceased, and the uterus decreased perceptibly in size. A definite anemia persisted, however. The patient continued with her work as a primary school teacher until she collapsed with abdominal pain. During the twenty-four hours which elapsed after her admission, her general condition improved markedly, but unmistakable signs of bowel obstruction developed. Laparotomy was performed thirty-six hours after the onset of the pain. The preoperative diagnosis was acute intestinal obstruction.

After the first blood transfusion of 500 c.c. the hemoglobin was 52 per cent; red blood count, 2,580,000; white blood count, 15,750 with 96 per cent neutrophils. A second transfusion of 550 c.c. of citrated whole blood was commenced at the beginning of the operation. Intrathecal anesthesia was used, giving 110 mg. of neocain to which was added 0.75 c.c. of pantocain.

Midline incision; numerous adhesions of omentum to the parietal peritoneum were seen. Several had to be freed before adequate exposure of viscera was obtained. Many coils of atonic, but otherwise good-looking, small gut were first



examined, after which the main mass of intestines was displaced cephalad by hot gauze packs. Approximately 750 c.c. of clear straw-colored fluid was aspirated from the pelvic cavity. No pus or free blood was encountered. A boggy, dark, beefy red loop of ileum 20 inches long was found doubled tightly on itself and bulging or rather herniating through an opening 2 cm. in diameter just below the right ovarian ligament as shown in Fig. 1. The gut apparently had entered the opening in an anteroposterior direction as shown. No attempt was made to pull the gut through the hole as it was obviously impossible due to edema. The roof of the tunnel consisted of the right ovarian ligament, mesial portion of right tube, and remnants of the right round ligament (mostly scar tissue replacement after Baldy type suspension). This roof was laid wide open with blunt-ended scissors, and raw ends were ligated and then oversewn with redundant peritoneum. No attempt was made to remove the distal portion of the right tube nor the right ovary. The released loop of gut was watched for a few minutes and regained much of its natural color. It was considered viable and was left alone. The uterus was seen to contain at least one and possibly more fibroids (Fig. 1). Nothing was done to the fibroids. Uterine attachments of both round ligaments were seen to be on the posterior surface of the uterus. They consisted at these areas of anchorage, of fibrous tissue, and had lost all resemblance to the original tissues. The left Baldy-Webster opening in the broad ligament was apparently closed. The abdomen was closed in layers without drainage.

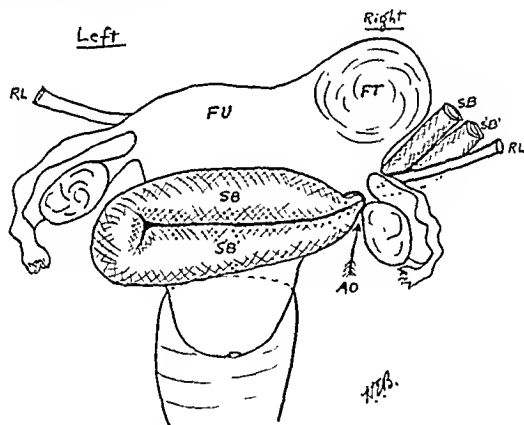


Fig. 1.—Case 17. *RL*, Round ligaments; *FU*, fundus uteri; *FT*, fibroid tumor; *SB*, *S'B'*, small bowel; *AO*, abnormal opening in broad ligament.

The patient tolerated the operation quite well, her condition being definitely better at the end of the procedure than at the beginning. Prior to incision, temperature was 100°; respiration, 22; pulse, 110 (thready). Lowest pressure reading was 80/30. After 1 c.c. of ephedrine by hypodermic, it rose to 126/80 and remained nearly at this figure until the end of the operation. Pulse at close of operation was 130 but regular and strong.

Convalescence was uneventful and she left the hospital on the seventeenth post-operative day in good condition. She has received subsequent intensive treatment for her anemia and is at present well and strong, working full time at her occupation of teaching school.

CASE 18.—Aged 62 years, Caucasian, para iv. Admitted March 1, 1931, to the Kahuku Plantation Hospital near Honolulu with the chief complaint of constipation and vomiting. For eight years she had been troubled with stubborn constipation,

accompanied frequently by severe pain in the left lower abdomen. During the week prior to her hospital admission, the bowels had moved normally. There followed a period of four days with no movement. She attempted catharsis but vomited the epsom salts as soon as they had been swallowed. That night she took an enema with good results and felt all right again until the night before admittance when she again vomited. Another enema following this gave good results.

She had never had any abdominal operations. She had had three cerebral accidents during the past few years, each one paralyzing her for a number of weeks, but apparently leaving no further residua. Persistent hypertension had been present for years. On examination the patient was noted to be quite obese and the heart was markedly enlarged to the left. Blood pressure was 192/90. There was a moderate systolic murmur and an occasional dropped heart beat. The abdomen was moderately distended, but no tenderness, masses, or rigidity was noted. Pelvic findings were negative. The white blood cell count was 6,700. The urine contained considerable albumin but no casts and was otherwise negative. An x-ray photograph of the abdomen showed stepladder fluid levels suggesting intestinal obstruction. The preoperative diagnosis was "partial intestinal obstruction probably due to malignancy with carditis and hypertension."

The patient was operated upon by Dr. H. T. Rothwell and Dr. J. E. Strode, by whose kind permission the case is here reported. A left rectus incision was made under drop ether anesthesia. Spinocain was first given intrathecally but was ineffective. A 4-inch loop of small intestine was found herniated through a congenital foramen in the left broad ligament. The gut had passed through the broad ligament from behind forward. The gut appeared viable and was pulled gently through the foramen, after which the aperture was closed by bringing its edges together. The patient died of cardiac decompensation thirty-six hours after operation.

#### SUMMARY AND CONCLUSIONS

Broad ligament hernia is one of the rarest of the internal hernias. Only 16 cases have been recorded in the literature to date. Two other cases are presented herewith for addition to the list. The leading predisposing causes of the condition are multiparity, the presence of congenital fenestrae or pouches in the broad ligament, or a preceding Baldy-Webster uterine suspension. Diagnosis is based on the symptoms and signs of intestinal obstruction.

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## PARADUODENAL HERNIA

J. W. SNYDER, M.D., MIAMI, FLA.

A SURGEON is due many surprises in abdominal exploration, but none is more startling than to open an abdomen for intestinal obstruction and find no intestine presenting within the abdominal cavity. Such a picture may be seen with acute obstruction of a paraduodenal hernia. All of the small intestines are contained within a retroperitoneal sac and, as the colon may be crowded entirely outside of the operative field, nothing but a smooth peritoneal covered mass can be seen by the operator. In the case which I will report, the only structure to be felt or seen was a smooth cystlike mass which completely filled the abdominal cavity. The rarity of the condition and the necessity of promptly recognizing its nature in order to meet the situation adequately have prompted reporting this single case.

CASE REPORT.—Mr. C., aged 51 years, first entered the Tuberculosis Pavilion March 2, 1938. In 1916 he had been diagnosed as tuberculous and was sent West where he lived for three years with apparent arrest of the process. He had a recurrence in 1920, at which time moderately far advanced pulmonary tuberculosis involving the entire left lung, with cavitation, was diagnosed. He was treated by pneumothorax and general measures during the following seven years; at one time he developed an effusion, but generally he was in a fair state of health. A recurrence of pulmonary activity with bloody sputum finally brought him to the hospital. He had lost 22 pounds in weight and was quite weak. Subsequent information obtained from his wife showed that for the past four years he had suffered from abdominal colic after meals. The attacks were severe, most often occurring at night. He found relief in the knee-chest position or from local heat applied to the abdomen, and by enemas. As soon as he felt a rumbling in the abdomen and was able to pass gas he was relieved. He found that mineral oil lessened the frequency of the attacks. He was never seen in an attack by a physician as home remedies had been effective.

The clinical findings on admission showed a positive sputum with a subsiding temperature and homogeneous density over the entire left chest due to thickened pleura from an old pleural effusion. The trachea was displaced to the left. The right lung showed a compensating emphysema and small lesions in the second and third interspaces. A permanent phrenic nerve paralysis on the left side was advised, to be followed by an upper thoracoplasty for the closure of cavities in the upper left lobe. On April 6, 1938, a phrenic exeresis was carried out without incident. His subsequent course was uneventful for seventeen days. Late in the evening of the seventeenth day he complained of indigestion and abdominal colic. Two enemas were fairly effective without relief of the pain. Emesis occurred and continued with gradual development of abdominal distention during the night. Stupor and all other measures were without effect and early the following morning the abdomen was distended and tympanitic with no cessation of pain or vomiting. Scout x-ray plates disclosed dilated ileum with fluid levels, so that the diagnosis of acute intestinal obstruction seemed

certain. He was immediately prepared for surgery. It is unfortunate that the roentgenologist did not have an opportunity to examine the films before operation as the distended loops of bowel were so peculiarly grouped together in a more-or-less circumscribed mass that it is possible the correct diagnosis might have been made pre-operatively.



Fig. 1.—Chronic pulmonary tuberculosis with cavitation and thickened pleura on the left.

Under spinal anesthesia combined with cyclopropane inhalations, a right rectus incision was made. On entering the abdominal cavity no intestines could be found in any part of the abdomen. The abdominal cavity was rather tensely filled with a mass resembling an ovarian cyst, which extended well up under the costal margin and down into the pelvis. Intestines could be seen beneath the surface of the mass. It was recognized as a retroperitoneal hernia but after prolonged search no point of entrance into the sac could be made out. The sac, therefore, was opened through an avascular portion and the intestines allowed to extrude from the sac. It was then found that the neck of the sac opened to the left and that the first portion of the jejunum was incorporated in its wall. The intestine was then reduced through the neck of the sac with some difficulty because of distention of the various loops. The

circulation of the bowel did not seem seriously impaired and there were no adhesions in the sac. Further examination showed that the superior mesenteric vessels were in the anterior margin of the sac and that the opening was placed between the first portion of the jejunum and the cecum, lying slightly to the right of the spine. All of the small intestine except a terminal two or three inches of the ileum was enclosed within the sac. The anterior margin of the neck of the sac was then sutured to the posterior abdominal wall close to the first portion of the jejunum, thereby closing the neck of the sac, care being necessary to avoid the superior mesenteric vessels. The opening first made in the wall of the sac was also closed by suture and the abdomen was closed with some difficulty. The patient's condition at the close of the operation



Fig. 2.—Scout film of the abdomen, showing dilated ileum over most of abdomen, but all confined within a circumscribed area.

was fair, showing an increase of pulse rate from 112 to 136. He was given 5 per cent glucose and acacia during the operation, and subsequent transfusions. Wangenstein drainage and an oxygen tent were employed, together with the usual postoperative measures used in intestinal obstruction. The drainage from the tube gradually changed from fecal to a clearer appearance and reasonable hope was held for recovery but two days after operation pneumonic consolidation of the right base of the lung terminated in death of the patient. Unfortunately an autopsy could not be obtained.

In retrospect we regret that our diagnosis was not more accurate and further that acute obstruction was necessary to call the condition to our attention. As previously stated, the history of intermittent partial intestinal obstruction was not obtained at the time of his admission to the hospital.

## ETIOLOGY

Neubauer in 1776 discovered "an exceptionally rare case of a peritoneal sac holding all of the small intestines." From this time the literature is rather profuse in the description of various folds and pockets scattered about the abdomen which were thought to be the possible points of origin of retroperitoneal hernias. It remained for Treitz in 1857 to bring order into the general thought by describing various fossae about the duodenojejunal junction which he thought were the probable beginnings of retroperitoneal hernias. He believed that these fossae were expanded and deepened by pressure and the peristaltic movement of the

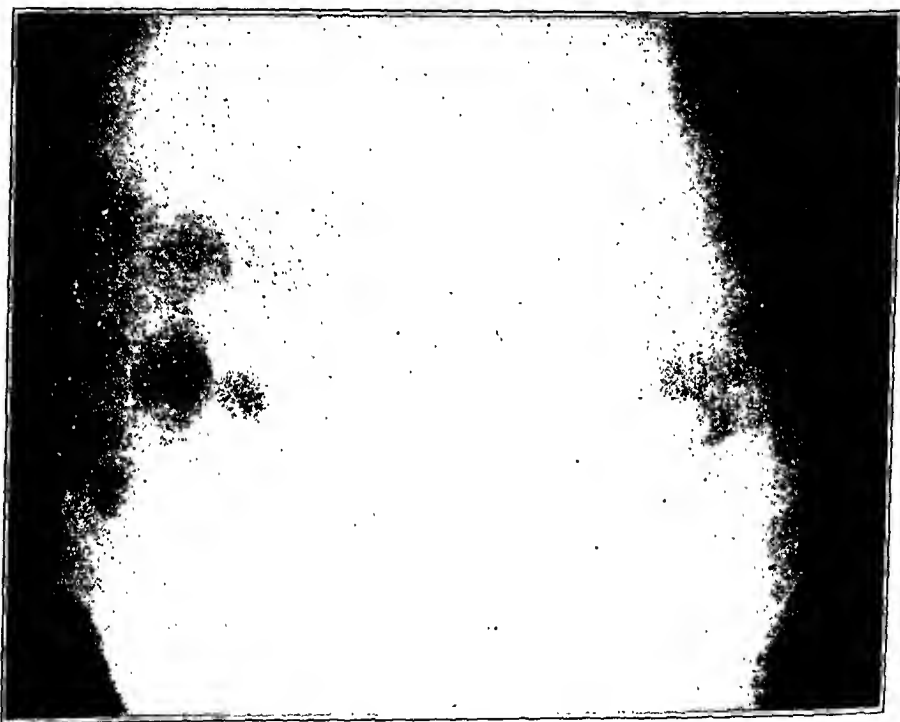


Fig. 3.—Patient in erect position, showing dilated ileum and fluid levels all confined within a circumscribed area.

intestine until a true hernia with a sac was produced. Subsequently authors have generally amplified this conception, the most noteworthy contribution being that of Moynihan on retroperitoneal hernias. He enumerated nine fossae located about the duodenojejunal junction, only five of which he considered of practical importance. He felt that the ultimate size of the hernia depended on the laxity of the retroperitoneal tissue and the extensibility of the peritoneum. Subsequent authors accepted this general idea as to origin without question, ascribing the development to a postnatal period, although Vogt described such a hernia in a newborn infant and Broesike in a child 14 days old.

It remained for Andrews in 1923 to question seriously this mode of origin. He felt that the entire conception was absurd and grotesque. To support his claims he held that:

1. Differential pressure in the abdomen is entirely lacking. All fossae or pouches are enclosed within the abdominal cavity, none extending outside the abdominal wall and therefore pressure at all points must be equal.

2. There are literally hundreds of similar folds and fossae in the peritoneum which rarely if ever are the site of hernias.

3. In all but a few cases the degree of herniation has been total or sub-total.

4. Vogt and Manski report hernia in the very young and the newborn.

5. The hernial sac never contains anything but small bowel. Omentum so commonly found in other hernias is strangely absent.

In brief, his opinion is that hernias are caused by a "congenital anomaly in the development of the peritoneum."

In Andrews' discussion of the embryologic development of the gastrointestinal tract, he postulated that, while the small intestine is developing rapidly from the original single loop, the colon is more retarded. As the colon finally passes across the abdomen from left to right, its mesentery forms the transverse mesocolon. The cecum grows even more slowly not starting its downward migration to the right iliac fossa until the hepatic flexure has been established. In its final position its mesentery becomes attached to and fuses with the posterior abdominal wall. If in the process the small bowel is caught beneath the mesentery of the advancing colon and imprisoned by the fusion of the colon itself to the posterior abdominal wall, all requisites for the formation of a right paraduodenal hernia would be fulfilled. Here the superior mesenteric and the ileocolic artery would lie in the superior margin of the neck of the sac exactly as is found in all right paraduodenal hernias. In a somewhat similar manner he explains the formation of a left paraduodenal hernia, only in this instance the small bowel is caught beneath the mesentery of the descending colon. Longacre has carefully dissected two cases of left paraduodenal hernias dying from other causes. He finds in the course of the blood vessels and in the presence of paraduodenal fossae which were not concerned in the hernia much to confirm Andrews' conclusions.

Brown in 1925 described a case of intraperitoneal right duodenal hernia which, together with a similar case of Sir Astley Cooper in 1807, have been considered as difficult if not impossible to explain as originating in the fossa of Waldeyer according to the explanation of Treitz. It is interesting that recently a third case in a 3-months-old infant has been carefully dissected by Paul and Hill and they find that "the present hernia did not commence in a fossa on the posterior abdominal wall at all, but in one on the side of the mesentery."



Apparently Andrews' ideas are gaining in favor although they are not fully accepted by all authors. Certainly the thought is logical and the presenee in the newborn of such hernias is diffienlt to explain on any but an embryologic basis.

#### DESCRIPTION

A right paraduodenal hernia, as previously stated, carries the superior mesenteric artery close to the margin of the neck of the sac and the opening of the sac points to the left. The ascending colon may lie to the outer side of the sac, may pass across its surface, or as in the case of Harris the asecending colon may lie along the superior margin of the sac with the cecum in the left hypochondrium. The variations in location apparently depend upon the laxity of the mesocolon or, stating the question in another manner, the degree of fusion with the posterior abdominal wall. While a right paraduodenal hernia commonly oeenpies the right side of the abdomen, Paul and Hill describe a right paraduodenal hernia which occupied the left side by reason of a rotation of the hernial sac to the left.

A left paraduodenal hernia has the opening of the sac pointing to the right. The anterior margin of the sac carries the inferior mesenteric vein and the ascending branch of the inferior mesenteric artery. Careful dissection by Callander and Longaere has shown that the mesentery of the descending colon beneath these vessels is particularly lax in the developing fetus and as the vessels offer resistance the invagination always occurs beneath these vessels. As a result the opening of the sac is always in this one partieular location. The descending colon lies to the outer side of the hernia, although it may be displaced medially. Some hernias contain only a few inches or feet of small intestine rather than the total length of the small bowel. There is no certain reason why only a portion of the bowel could not be invaginated into the mesocolon rather than the entire length. No instance has been reported of colon or omentum being found in such a sac. Pericecal hernias of very rare occurrence could be accounted for in a similar manner.

Broesike emphasized a fusion of the first part of the jejunum with the posterior abdominal wall. In these cases only the efferent loop of the gut may be seen to pass through the hernial orifice, the afferent loop entering retroperitoneally from above. Moynihan makes this the basis for division of right paraduodenal hernias into two types to which he assigned involved nomenclature, depending on whether the first portion of the jejunum was free or retroperitoneal. It would seem that the only logical way to explain this condition is on an embryologic basis. Certainly a retroperitoneal jejunum is difficult to explain as a postnatal development.

Baumeister and Hanchett recently have reported a case of right paraduodenal hernia in which the opening of the sac pointed to the left through which the intestines entered, as should be expected, but the sac

also had a second opening on the right lateral wall outside the colon. They feel that this circumstance is more in line with the theory of Treitz and is difficult to explain by Andrews' conception. In their case they state that the patient received a severe blow on the abdomen from the steering wheel of her car when the car turned over once and one-half times seven years before the onset of her present trouble. It is difficult to avoid the conclusion in their case that the lateral opening of the sac was the result of a rupture from trauma and should not be considered in etiology.

#### OCCURRENCE

Paraduodenal hernia may be observed at any age. Its occurrence is relatively rare. In 1930 Masson and McIndoe were able to report a total of only 3 cases from the Mayo Clinic up to that time, 1 left and 1 right, both found at autopsy and a third operated upon with recovery. Brown in 1915 reported a total of 32 right-sided cases, in 15 of which operation had been performed, with recovery in 4. The other 17 cases were found at necropsy. Credit for the first successful cure of a right-sided hernia belongs to Newman in 1898 and the second to Carson in 1912.

Byron in 1935 reported 43 cases of right paraduodenal hernia, of which 26 were operated with 14 recoveries and 12 deaths. He also reported 162 cases of left paraduodenal hernia from a survey of the literature.

Left-sided paraduodenal hernias are approximately four times as frequent as right and statistics also indicate that the operation for right paraduodenal hernia is particularly hazardous, being five times more fatal than for the left.

#### DIAGNOSIS

In 1923 Nagel reported that not a single case of right-sided hernia had been diagnosed before operation and of 91 cases of left duodenal hernia collected by Pikin only 3 were clinically diagnosed. Exner in 1933 states that the credit for the first preoperative diagnosis of a right-sided hernia should go to Taylor who made the diagnosis in one of his cases by x-ray. Exner's report in 1933 was the second diagnosis correctly made.

In certain cases the symptoms have been entirely in abeyance and the condition entirely unsuspected at necropsy. In others symptoms of a vague dyspepsia suggesting gastric or gall-bladder pathology may induce prolonged medical therapy. When the symptoms are more acute, they assume the picture of subacute or acute partial intestinal obstruction. Intestinal colic, particularly after a heavy evening meal, may precipitate an attack. Vomiting is uncommon, except in complete obstruction. The vomitus contains bile. Fecal vomitus is rarely seen because of the high obstruction. Repeated attacks of colic are associated with abdominal soreness and distention relieved with the passage of gas along the intestine. Visible peristalsis and a palpable resonant, gurgling, balloon-like

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tumor in the lower abdomen, later involving the entire abdomen, are considered by Moynihan to be the most significant diagnostic signs. The x-rays in our case should have made the diagnosis even without the use of barium as the intestines, although definitely obstructed, remained circumscribed in a definite limited oval area. Exner says that the clumped appearance of the intestinal coils, as if they were contained in a bag, is the most characteristic sign of right paraduodenal hernia.

#### TREATMENT

The treatment is surgical. Fortunately several cases have been explored for pathology in the absence of obstruction in which situation the hernia can be handled with some ease. In the presence of acute obstruction the situation is quite different. It is essential first to recognize the pathology and secondly, to determine whether a right or left hernia is present. If the sac can be found it may be possible, with gentle dilatation of the neck of the sac, to reduce the hernia. Caution should be maintained not to injure the important vessels lying along the anterior margin of the sac. Adhesions about the neck of the sac are frequently encountered. If, as in our case, the neck of the sac cannot be readily localized the sac may be opened through an avascular portion; the contained intestines extruded and the neck of the sac approached from the inside. Strangulation and necrosis demand resection of the bowel. Adhesions between the loops of the bowel are rare except at the neck of the sac. The neck of the sac should be closed after freeing the bowel to prevent recurrence. Recurrence has been reported in two cases where this has not been done. If reduction is not possible the neck of the sac should be enlarged as much as possible to prevent obstruction. The fortunate case is one with a wide neck and no adhesions to divide, for this permits easy reduction with minimum shock and a good chance for recovery.

#### SUMMARY

A case of right paraduodenal hernia has been presented which had a long history of intermittent intestinal obstruction and a final severe total obstruction. The long history of advanced pulmonary tuberculosis greatly obscured the picture and the further fact that the patient was never seen in an attack by a physician partly mitigates the oversight. The flat plate of the abdomen should have been of greater diagnostic value, but it was not recognized as indicating more than an acute intestinal obstruction. The thought occurs: Could the phrenic excrescence done seventeen days before the terminal obstruction have been a factor in producing the final picture?

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Normally, it is completely or partially covered by the arching fibers of the internal oblique muscle. When these fibers contract, they tend to straighten out their arch and lie in parallel apposition to Poupart's ligament, thus acting as a sliding trap door. McGregor has even gone further and demonstrated the existence of a true sphincter, consisting of fibers of the internal oblique, at this point. He found it particularly well developed in the dog. However, I have failed to find any sufficient bundle of muscle fibers which can be dignified by the term of sphincter, either in vivo or after a careful search in the human cadaver; although there are fibers of different amount and caliber passing down along the cord, parallel to Poupart's ligament. Furthermore, considering the oblique direction of the inguinal canal, passing as it does at different levels through the different layers of the abdominal wall, it would seem that a trap-door closure would be more effective than a sphincteric one, which, in addition, would tend to have a deleterious constricting effect upon the vessels of the cord.

Variations in the position of these arching fibers of the internal oblique in relation to the internal ring have been pointed out by anatomists. Cherner has recently published illustrations showing that the further away from the anterior iliac spine the muscle takes its origin, the less chance there is for adequate protection of the space bounded by the anterior superior spine, the pubic spine, and Poupart's ligament. There are three factors which might account for these variations: first, the character of the embryologic development of the abdominal muscle plate, which permits the muscle component to grow cephalically while the fascial portion remains fixed at the inguinal region; second, the widening of the pelvis with the flaring out of the ilia; and third, the assumption of the erect posture. Thus a change occurs in the direction of Poupart's ligament from an almost vertical to an oblique one, while the fanlike expansion of the internal oblique muscle takes place upward and laterally.

The operation herewith reported has as its rationale: first, elimination of the cause of the hernia, if possible; second, narrowing of the lumen of the opening in the transversalis fascia; third, restoration of the internal oblique muscle to a position in which it can act as a buffer at the internal ring. This muscle restoration is accomplished by lengthening its fascial attachment to Poupart's ligament, thus dragging the belly of the muscle more laterally, without interfering with its normal contractile power. More permanency is secured by the use of fascial strips taken directly from the field of operation, as McArthur advocated years ago, without the necessity of invading another field and still without sacrificing any tensile strength.

Attaching the belly of the muscle to Poupart's ligament as is done in the Bassini operation and all modifications is wrong in principle, as this fixation immediately interferes with the functional activity, resulting in

# INGUINAL HERNIOPLASTY: A NEW MODIFICATION

## REPORT OF 107 CASES

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(From the Surgical Service, Hospital for Joint Diseases)

FEW subjects have a more voluminous literature than that of hernia. There are several reasons for this. First, it is known to exist throughout the whole animal kingdom, true hernia having been observed in fish, amphibia, reptiles, birds, and all so-called lower animals. Second, art and literature show the existence of hernia in ancient man. And third, the result of operative intervention is very far from satisfactory, recurrences ranging anywhere from 7 to 50 per cent in different types of hernia. I would hesitate to add to this literature unless I were convinced that the basic concept and operative technique required radical revision.

The cure of inguinal hernia, like that of any other lesion, depends upon the eradication of the cause and the permanency of the repair. The etiologic factors can be classified thus:

### 1. Anatomic

A. Patent processus vaginalis.

B. General or local tissue weaknesses; e.g., chronic disease, split aponeurosis, weak transversalis fascia

C. Disproportion between the abdominal capacity and contents; e.g., large tumor or ascites

D. Long or low attached mesentery

E. Large internal ring

### 2. Mechanical

Increased intra-abdominal pressure from within or without

### 3. Physiologic

Inadequate trap-door action of the internal oblique muscle. This paper will deal mostly with this physiologic inadequacy and method of correction

While the point of exit of the indirect inguinal hernia, the superficial ring, has been overstressed, the site of origin, the deep ring, has been unduly neglected. Unfortunately the internal ring is rather inaccessible, corresponding to a site half an inch medial to the midpoint of a line connecting the symphysis with the anterior superior spine. Even an exceptionally long finger could only reach it with considerable difficulty and trauma. Nevertheless, the main problem in the cause and cure of the indirect inguinal hernia is the determination of the tonus of and protection afforded to this opening in the transversalis fascia.

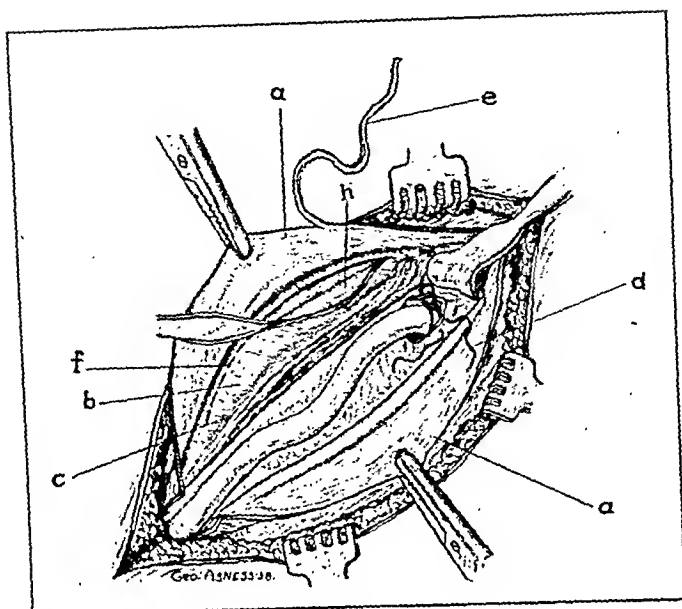


Fig. 1.

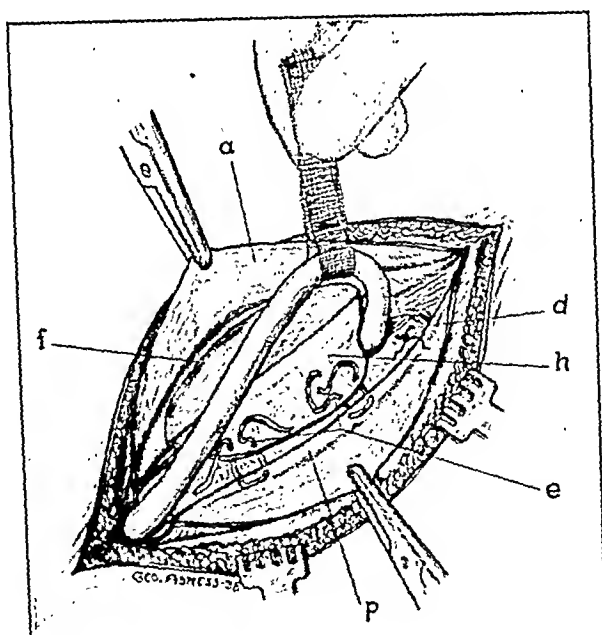


Fig. 2.

Figs. 1 and 2.—a, Aponeurosis external oblique muscle; b, aponeurosis internal oblique muscle; c, internal oblique muscle; d, suture through edge of internal ring; e, fascial suture taken from external oblique aponeurosis; f, incision in aponeurosis internal oblique; h, fascial flap from internal oblique aponeurosis; p, Poupart's ligament.



the usual atrophy of disuse. And later, when or if the sutures are partially or completely absorbed and the muscle tends to assume its former position, its contractile power is even weaker than before the operation, thus favoring recurrence. To the argument that the muscle fixation tends to build up the floor of the canal, it can be stated first, that in an indirect inguinal hernia there is no defect of the floor; and second, that nowhere in the human economy is the muscular system used for such a purpose, its function being locomotion, motion, sphincteric control, and stabilization.

#### IMPORTANT STEPS IN HERNIOPLASTY

1. Incision: About 2 inches longer than the usual incision.
2. Splitting of the aponeurosis of the external oblique, from the external ring to the muscle fusion.
3. Splitting of cremaster fibers to expose the sac medially to the cord.
4. Retraction of the cord.
5. Thorough isolation of the sac by sharp dissection.
6. High ligation of the sac after defining the edge of the transversalis fascia at the internal ring with clamps.
7. Mattress sutures, narrowing the internal ring cephalad to the cord.
8. Excising a strip of fascia from the medial leaf of the external oblique aponeurosis which is used to make two fascial sutures.
9. Exposure of the internal oblique aponeurosis at its junction with the external oblique aponeurosis.
10. Incision of the internal oblique aponeurosis at and parallel to its line of fusion with the external aponeurosis to well above the level of the internal ring.\*
11. Reflection of the internal oblique aponeurosis laterally.
12. Suturing the reflected internal oblique aponeurosis to Poupart's ligament with three chromic catgut sutures and the fascial prepared strips.
13. A chromic catgut or fascial suture also placed above the internal ring.
14. The two edges of the external oblique aponeurosis are brought together with chromic catgut sutures.

In most cases the cord is transplanted, although it is not essential in all cases. The external oblique aponeurosis is resutured, usually without any tension, notwithstanding the previous removal of some of its structure. The skin is closed with interrupted silk sutures.

#### DIRECT INGUINAL HERNIA

The mechanical problem in this type of hernia is quite different from that of the indirect variety. In fact, many surgeons do not consider

\*In direct hernias at this stage a free edge is made of the transversalis fascia and this free edge is included with the sutures, through the internal oblique aponeurosis, and sutured with it to Poupart's ligament.

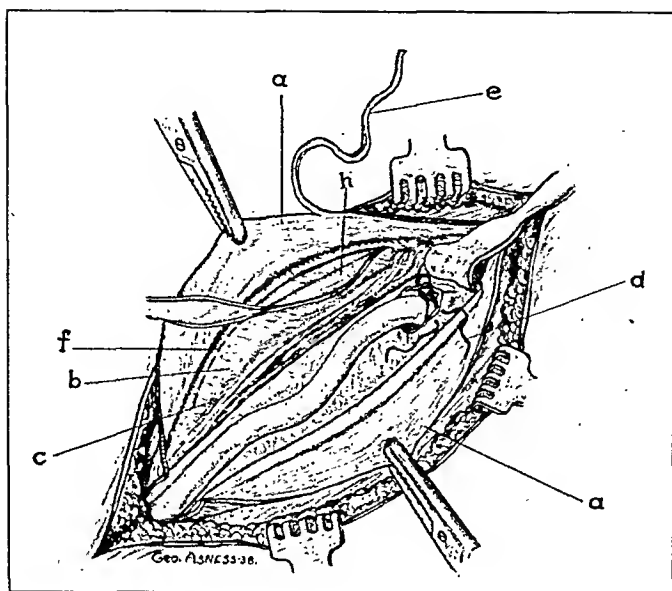


Fig. 1.

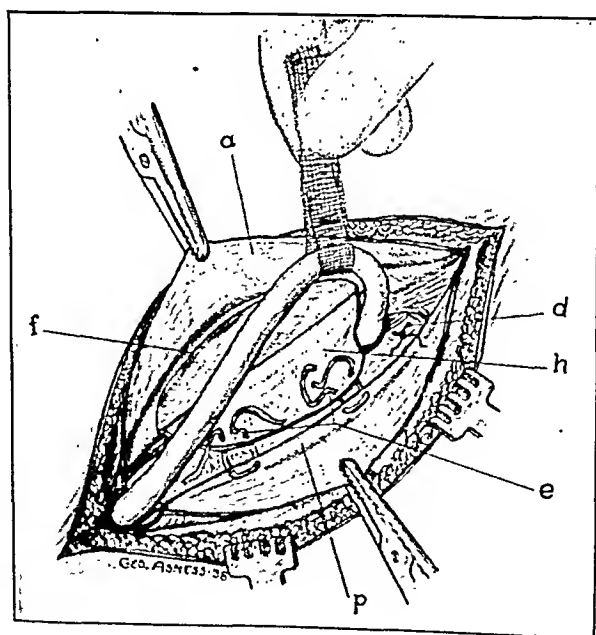


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it a hernia in the true sense. In the large majority of cases there is simply a relaxation of the distal third (inguinal triangle) of the floor of the inguinal canal. But not infrequently there is a distinct aperture and it is this type that may and does become strangulated. Preoperatively it is impossible to determine which type one is dealing with.

The floor consists normally only of peritoneum and transversalis fascia, the latter covered over and concealed by loose areolar tissue and at the lower angle devoid of any overlying muscular or aponeurotic protection. This fascia, however, is absent at the lateral third of the floor, at which point the fascia dips down into the pelvis.

In the presence of this unprotected area one has a right to expect direct hernias occurring more frequently than the indirect, the reverse of which is the truth. This discrepancy never has been explained satisfactorily. Anatomie variations may be the answer. Whereas normally the internal oblique muscle is inserted into the pubic spine, in a certain number it is inserted into the rectus sheath at variable distances above the spine, thus leaving the inguinal triangle without any muscular protection. Dimensional studies of this triangle have been made both in the cadaver and at operation. Anson and McVay found the median border varied from 0.5 to 9 cm. in length. Polya gives figures up to 7 cm. Andrews' average figure was 5 cm. According to Ssosan-Jaroschewitsch, a greater muscular defect existed in the direct than in the indirect hernias, and the lower fibers of the internal oblique muscle approached nearer a right angle with the rectus sheath.

Based on these and his own observation, Zimmerman in a recent article stated: "From these repeated observations, the conviction grows that the underlying predisposing anatomical basis for direct hernia consists of a congenital absence of adequate muscular support for the lower portion of the inguinal canal. . . . Inasmuch as there are no methods by which muscle can be made to grow where it is deficient, the defect must be repaired by some type of fascial plastic procedure."

With the first part of this statement the writer thoroughly agrees and for the past five years has based his anatomical surgical procedures on this very fact, as stated above. The second part of the statement cannot be accepted as a proper corollary to the first.

*Operation.*—The object is reinforcement of the floor of the canal, first by closing the aperture in or taking up the slack of the transversalis fascia and second by transplanting the internal oblique muscle nearer Poupart's ligament particularly at its lowest median portion. The approach is the same as for the indirect variety; the cord is retracted well to the side and the floor of the canal exposed from the deep ring to the symphysis. It is most important to clear the transversalis fascia of its overlying areolar tissue, going well underneath the internal oblique muscle. The lateral limitations of the fascia come clearly into view. It

is not sufficient to reduplicate this fascia to Poupart's ligament as many do. A longitudinal incision must be made through it, not including the underlying, nonadherent peritoneum, unless the latter is distinctly sacculated or very large, in which event the excess of peritoneum is excised. The free edge of the transversalis fascia, together with the cut edge of the internal oblique aponeurosis, is then sutured to Poupart's ligament with two or three fascial strips taken from the external oblique aponeurosis and a few chromic sutures. Particular attention is paid to the lowest point of the triangle and all effort made to avoid any tension. The cord overlies the new bed. The external aponeurosis and skin are then sutured.

#### RECURRENT HERNIAS

It was in this type that we experienced the greatest satisfaction. The principle and technique were essentially the same as in the primary hernias. Fortunately the aponeurosis of the internal oblique was always available as it had not been utilized or interfered with at the original operation. If difficult to expose at the site of operation owing to adhesions, it was traced down from above. In most cases the external oblique was so fibrous or foreshortened by imbrication that it was not available for fascial strips. In that event only, strips were taken from the fascia lata but not used in Gallie weaving fashion approximating muscle to Poupart's ligament but used as mattress sutures approximating the structures indicated above. In the early series silk was used to reinforce the knots of the fascial sutures. As discharging sinuses persisted for six months, in two cases until expulsion of the silk, the latter has been discontinued and catgut substituted.

Two of the cases operated upon for recurrences had been operated upon three times previously, and two of them were of the sliding variety.

#### STATISTICS

One hundred and twenty-six hernioplasties were performed without any selection of cases, many of which appeared very unfavorable. Thirteen patients had a follow-up period of less than a year. Four cases have been lost track of and 2 have died, leaving 107 cases. There were 62 indirect hernias, including 1 sliding hernia; 26 direct; 6 direct-indirect; 13 secondary (recurrences), including 5 indirect (two sliding), 7 direct, and 1 Spiegel.

##### TIME ELAPSING SINCE OPERATION

YEARS	4	3	2	1
CASES	17	28	29	15

##### AGE DECADE

10-20	21-30	31-40	41-50	51-60	61-70
5	18	28	17	16	5

Total 89 patients

Sex.—86 males, 3 females

Deaths.—1 due to massive gangrene of urinary bladder  
1 due to meningitis, three months postoperatively

Recurrences.—Total, 3.75 per cent

A. Indirect, 0

B. Indirect-direct, 0

C. Direct, 3 cases (11 per cent)

1. Age, 31 years; recurrence left side noticed one and one-half years postoperatively, weak internal oblique fascia noted at operation. Recurrence right side (Bassini) one year postoperatively.

2. Age, 61 years; recurrence one side two years postoperatively; heavy work, superintendent of building.

3. Age, 49 years, one side recurrence, two years postoperatively.

D. Secondary, 0.8 per cent, 1 case

1. Age, 51 years; left side, parietic, recurrent sliding, three and one-fourth years postoperatively.

Note.—All recurrences originally bilateral hernias, none infected.

#### CONCLUSION

A plea is made for a more logical concept of inguinal hernia.

The importance is stressed of the internal ring and internal oblique muscle in indirect hernia; of the cut edge of the transversalis fascia in the direct variety.

Result in indirect hernia to date seems perfect; in secondary recurrences very excellent; in direct hernia, while there is a definite advance, there is still room for improvement.

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# THE RESULTS OF TREATMENT IN CANCER OF THE PROSTATE

## A REVIEW OF 275 CASES

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School, University of Minnesota)*

### INTRODUCTION

THE outlook in cancer of the prostate is admittedly grim and has changed little with the development of modern surgery. Caulk has had no cures in 203 cases; Dolan found no ten-year cures in canvassing seventy urologists in 1937. There are several definite reasons for the poor prognosis:

1. The growth usually originates at a distance from the urethral lumen, Moore finding its origin in the posterior lobe in 73.7 per cent at necropsy.

2. Carcinoma of the prostate usually grows slowly, Chwalla having reported two patients who lived  $7\frac{1}{2}$  and 8 years, respectively, after cystostomy. This slow growth leads to the very gradual development of obstruction to urination, and to a corresponding hypertrophy of the detrusor which compensates for the obstruction and postpones subjective symptoms until relatively late.

3. Cancer and benign hypertrophy have their onset at about the same age and present the same symptoms; the patient is likely to accept them as the inevitable accompaniment of old age and to defer consulting a physician until they become intolerable.

As a consequence, local extension usually has attached the prostate to the surrounding structures and metastasis has often taken place by the time medical advice is sought. Barringer found only 16 cancers apparently confined within the prostatic capsule in 351 consecutive cases. Bumpus found metastases to bone in 24 per cent and Ferguson in 30 per cent of the patients x-rayed when first seen. Another bar to cure is the tendency of these tumors to invade the perineural sheaths in the pelvis; such invasion was found by Keyes and Ferguson in 52 per cent, and by Graves, Warren, and Harris in 100 per cent at autopsy.

### INCIDENCE

To add to the gravity of the problem, the incidence of cancer of the prostate is apparently increasing. It causes 20 per cent of all obstructions at the vesical neck (Young); it is responsible for 0.6 per cent

of all deaths, and for 4 per cent of those due to cancer in the male (Caulk). Moreover, prostatic cancer has been found at necropsy in 14 per cent of men of all ages by Rich; in 21 per cent of those past 41 years of age by Moore; and in 23 per cent of males past 70 years of age by Muir. Duff found that the death rate from prostatic cancer among the industrial policyholders of the Metropolitan Life Insurance Company increased from 0.8 per hundred thousand in 1917 to 3.7 in 1928.

There are at least two factors in this increase. First, the development of transurethral resection has heightened interest in all disorders of the prostate and lessened the seriousness of prostatic surgery in the patient's mind, so that many more are submitting to operation instead of resigning themselves to suffering; one gets, therefore, a much more accurate idea of the true incidence of prostatism than one could fifteen years ago.

The second important factor is the increase in longevity which has occurred in the last quarter century, since the frequency of prostatic cancer rises with age; Rich found the lesion in 37 per cent of autopsies on patients between 76 and 80 years of age. The Metropolitan Life Insurance Company has observed that the life expectancy from birth of its industrial policyholders had increased from 46.6 years in 1911 to 60.7 years in 1937. The population as a whole has shared in this increase; during the same time, the birth rate has fallen. These two factors have augmented the proportion of the population living in the cancer age, thus causing a great increase in the number of cases of cancer without increasing its proportionate incidence in any age group.

#### ETIOLOGY

The cause of the disease is not known. None of the numerous theories thus far advanced has been proved. It is often attributed to irritation from prolonged infection; the great frequency of prostatitis makes this a most difficult question. Hryntschak has described multiple foci of regeneration in the prostate which he regards as perhaps postinflammatory and probably precancerous; they are more common in the areas of predilection for cancer. The question of endocrine influences, of course, must be mentioned in this day and age; it remains to be studied.

#### DIAGNOSIS

Diagnosis is usually easy but is subject to a number of pitfalls, especially in early or small lesions. If stony hardness and fixation have developed, there is little danger of confusion except with tuberculosis and calculi; to confuse these lesions with cancer is usually due to carelessness rather than to ignorance. The small, hard nodule may require biopsy for satisfactory identification unless one feels, as many

do, that treatment even of early cases is of little use; in this event, observation over a period of time usually will clarify the diagnosis. If one agrees with Young that radical operation is of great value in early cases, one must expose and excise the suspicious area for "fast frozen" section and employ radical perineal prostatectomy if cancer is found.

The value of aspiration biopsy is limited by the ability of the pathologist to interpret the scanty material thus collected. While Keyes and Ferguson had satisfactory results in 86 per cent, this performance is probably difficult to duplicate. If positive, it is conclusive; if negative, valueless. The last statement applies with equal force to biopsy by transurethral resection; the frequent presence of benign hypertrophy between the urethral lumen and the cancer often leads to error, especially in small lesions close to the true capsule, since the cancer itself may escape excision. The presence of osteoblastic metastases in bone is diagnostic but of hopeless import; the same is true of the presence of metastatic cancer in removed lymph nodes.

With all of these measures available, the incidence of error ought to be low in the hands of the careful observer, especially if routine sections are made of all material removed at operation in order to detect the occasional cancer which cannot be palpated because it is surrounded by benign hypertrophy.

#### TREATMENT

As is evident from the discussion of prognosis, treatment usually fails to effect a cure. Factors already discussed usually postpone the discovery of cancer of the prostate until too late for complete removal. Nevertheless, a good deal of palliation can be secured by thoughtful treatment. The methods in general use may be classified as follows:

##### A. Curative

1. Radical prostatectomy
2. Conservative prostatectomy (enucleation of small "concealed" cancer)

##### B. Palliative

1. Diversion of the urine
2. Irradiation
3. Surgery
4. Combinations

The chief obstacle to cure is the low incidence of localized cancer. Barringer found only 16 (4½ per cent) in 351 cases, and Colston reported that Young performed but 36 radical operations in 1,040 cases (3.4 per cent). Nonetheless, Young has had excellent results in the operable cases: 50 per cent of five-year cures, and freedom from re-



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5-year survivals, but by no stretch of the imagination can the results be called satisfactory; the patients are uncomfortable and none is cured.

Irradiation has long had its advocates; x-ray is simplest in application; it produces a temporary aggravation of symptoms when obstruction is at all severe; it is not ordinarily applicable to complete retention; it produces a temporary but annoying irritation of the skin and rectum when used in adequate doses. Dolan, in questionnaires returned to him by 63 urologists in 1936, found no instance of a 10-year cure from its use, and but five 5-year cures. It is useful chiefly as an adjuvant to radium and in relieving temporarily the pain from metastases to bone and from infiltration of nerve sheaths. Leddy and Gianturco found 3 patients completely and 21 considerably relieved for from 1 to 7 months; 16 were not benefited. Variations in the technique of application make the evaluation of results difficult.

It is at present rather generally agreed that the use of radium, especially when supplemented by x-ray, often causes shrinkage of the gland with alleviation of the symptoms after an initial aggravation, although Bumpus in 1926 found that patients treated with radium were never cured and lived only one-third as long as those treated by cystostomy. The expense and danger of application of radium by the external route has led to the widespread use of interstitial irradiation, with gold seeds of radon replacing the element itself because the former do not have to be removed. Barringer was able to control about 10 per cent of cancers for five or more years by the use of interstitial radon plus high voltage x-ray. While the seeds may be embedded directly into the exposed prostate, they are usually inserted through the intact perineum by means of special trocars. The inaccuracy of this method is more than compensated for by the lack of complications and by the shortened hospital stay. Of the two operative approaches, the perineal is to be preferred because the urethra is not opened. The suprapubic exposure lately advocated by Keyes and Ferguson is likely to be followed by a fistula if any considerable obstruction is present. However, their report that 14 of 41 patients (34 per cent) were living more than 3 years after treatment deserves attention.

The use of transurethral resection for the relief of obstruction in inoperable cases is too recent to permit wholly satisfactory evaluation, but one gets the impression that it is widely employed. It has been condemned as unsurgical to remove a portion of a malignant growth and it has been alleged that healing will not take place, while recurrence will be prompt. Metastasis is said by some to be favored thereby. Nevertheless, obstruction can be relieved in nearly all cases; the patient is neither encumbered nor discommoded by tubes or bottles; failure of the cut surface to heal is of but little moment if the patient can void comfortably; metastases will occur sooner or later

current obstruction in the remainder; Smith has had substantially the same results. Neither its mortality of 11 per cent nor the fact that many patients are incontinent after radical perineal prostatectomy destroys its value, since it offers the only hope of cure and the sole reasonable guarantee against recurrent obstruction to urination. Although 50 per cent of five-year cures in operable cases becomes 1.7 per cent of all cases when allowance is made for the rate of operability, the operation deserves more frequent employment since it alone offers any real hope of cure. To do so requires, of course, earlier diagnosis.

Radical suprapubic prostatectomy is, for anatomic reasons, more difficult to perform; it does not permit exploration and biopsy of suspicious nodules in the posterior lobe, and Marion claimed but 3 apparent cures in 48 cases. It is, therefore, but little used.

Enucleation of the cancerous prostate, whether suprapubic or perineal, may be regarded as curative only in those rather rare cases in which the tumor is wholly surrounded by benign hypertrophy with which tissue it may be enucleated. The diagnosis is usually missed clinically but made pathologically. The occurrence of this "ocent" cancer has been used as an argument against the employment of transurethral resection on the basis that enucleation will cure patients with this type of lesion while resection will obviously fail to do so. This argument is indefensible because of the incidence and rate of cure of this type of cancer. Von Illyes found 27 of them in a group of 354 prostatic cancers (8 per cent). In a series of 91 such cases, Cunningham, Hirsch and Schmidt, von Illyes, and Bugbee had 27 per cent of 2- to 5-year survivals. Thus not more than 27 per cent of 8 per cent of all prostatic cancers (2.1 per cent) may be "cured" by this enucleation. This percentage is further reduced by the fact that survival for 2 to 5 years is by no means synonymous with cure.

The solution, of course, lies in early diagnosis which becomes possible only when routine rectal examinations are made in all elderly men, or in those rare instances in which a small cancer is associated with a benign hypertrophy which surrounds the cancer and produces obstruction; and then only if the cancer is discovered during the operation so that radical excision may be employed.

The results of palliative procedures are not impressive. Catheterization is not even palliative; the bladder usually becomes infected, necessitating more frequent catheterization; suffering is ordinarily intense before death occurs.

Suprapubic cystostomy is more satisfactory if one overlooks the inconvenience of the necessary tube and bottle; the patient is permitted to live in reasonable comfort so far as the bladder is concerned until the tumor occludes the ureters or kills by dissemination. Bumpus found that postoperative life averaged 57 months with 5 per cent of

5-year survivals, but by no stretch of the imagination can the results be called satisfactory; the patients are uncomfortable and none is cured.

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The use of transurethral resection for the relief of obstruction in inoperable cases is too recent to permit wholly satisfactory evaluation, but one gets the impression that it is widely employed. It has been condemned as unsurgical to remove a portion of a malignant growth and it has been alleged that healing will not take place, while recurrence will be prompt. Metastasis is said by some to be favored thereby. Nevertheless, obstruction can be relieved in nearly all cases; the patient is neither encumbered nor discommoded by tubes or bottles; failure of the cut surface to heal is of but little moment if the patient can void comfortably; metastases will occur sooner or later

if operation is omitted; and the patient after resection may secure the benefits, if any, of all types of irradiation.

Bugbee operated upon 52 patients by the transurethral route without an operative death; all were relieved of their retention. Nine died of cancer and 3 of heart disease in from 12 to 44 months; 40 were living from 1 to 48 months; 3 had required reoperation, 2 for recurrent obstruction and 1 for hemorrhage.

Caulk was able to relieve obstruction to urination in 77 per cent of 129 cases. Thirty per cent lived 3 years; 18 per cent, 4; and 5 per cent, 7 years.

Jacobs has reported 15 cases so treated; 4 died of cancer in 3 to 20 months; 3 were not relieved; and 7 were free from obstruction to urination after 1 to 33 months.

Thompson and Emmett followed 107 patients treated with the knife punch with 1 operative death (0.9 per cent). Fifty-six were living from 6 to 48 months, and 51 had died, 24 during the first year after operation; 11 had required reoperation for recurrent obstruction after varying intervals. Most of the survivors were in satisfactory condition so far as urination was concerned.

Partial prostatectomy will relieve obstruction by permitting enucleation of a coexisting benign hypertrophy, or excision with knife or diathermy of the obstructing portion of the cancer itself; in other words, it offers the same benefits as does transurethral resection but at a much greater cost in terms of morbidity and mortality.

Swan and Mintz have reported the average hospital stay for suprapubic prostatectomy to be 14 days before and 30 days after operation; in contrast to this, Thompson has been able to omit preoperative preparation in 60 per cent of patients subjected to transurethral resection and puts the postoperative stay in the average case at 5 days.

The risk of transurethral resection is so much lower than that of partial prostatectomy as to demand its use on that basis alone. Colston found the mortality of partial perineal prostatectomy in 320 cases of cancer to be 6.6 per cent, far lower than can be expected with the suprapubic operation, but from three to six times that of transurethral resection (Caulk, Thompson, Davis).

It is thus apparent that transurethral resection is the operation of choice for the relief of retention of urine in those cases of cancer which cannot be removed in their entirety.

#### REPORTS OF CASES

The diagnosis of carcinoma of the prostate was made at the University Hospital 275 times from April 1, 1930, to Dec. 31, 1936. The first date was selected because it marks the beginning of my experience; the second, to make certain that at least one year had elapsed since the beginning of treatment in the last case. The following plan

determined the type of treatment used during this period; radical perineal prostatectomy was regarded as the preferred treatment, but was little used because, in a charity service, very few patients are seen early enough to permit its application. In those cases exhibiting local extension or metastases, the degree of urinary retention governed the method of treatment. If it was slight or absent, irradiation was employed, starting with the implantation through the intact perineum of radon in gold needles with a 0.3 mm. wall. This was followed by a course of high voltage x-ray therapy given by Dr. Karl W. Stenstrom, who varied the technique from time to time. In all, 200 kv. were used with a filter consisting of 1 mm. each of copper and aluminum and a half value layer of 1.3 mm. of copper. The target skin distance was 70 cm.; the field, 18 by 20 cm.; and the rate, 20 roentgen units per minute per field.

Up to 1934, an anterior and a posterior field were used, giving 4 to 6 treatments in 7 to 11 days, totaling 800 to 900 r. per field. The maximum dose to the prostate was calculated to be 1,200 r.

From 1934 to 1936, right and left lateral fields were also used, and the number of treatments was increased so that four weeks of treatment were required with a total dose of 1,100 r. to each field. The calculated dose to the prostate was 2,200 r.

Since 1936 the technique has been altered to include a perineal and right and left posterior oblique as well as anterior and posterior fields; lateral fields have been used if the diameter of the pelvis exceeded 20 cm. The dose to the prostate has been increased to 2,600 r. (with scattering) in four weeks. Since this last change was inaugurated, the x-ray therapy has preceded the radon.

If retention of urine was severe, cystostomy was often employed before irradiation during 1930 and 1931 and was followed by irradiation; thereafter it was treated by transurethral resection, except in a very few instances in which the resectoscope could not be inserted or in which the general condition contraindicated resection. When the latter was used, it was planned to supplement it by irradiation after an interval of six weeks to allow the postoperative reaction to subside. Some of the patients failed to return for a part or all of the irradiation, and thus afforded small control series for comparison.

Partial prostatectomy was carried out deliberately for cancer in only a few instances; the remaining prostatectomies were done for what was thought to be benign hypertrophy but which proved to be carcinoma on section; since 1932 nearly all of these cases have been treated by the transurethral operation.

In most instances prostatectomy was also followed by irradiation either with radon, with x-ray, or with both.

One hundred and twelve patients were treated by irradiation only; 102, by transurethral resection with or without irradiation; 29, by

partial prostatectomy with or without irradiation; 11, by cystostomy supplemented in 8 by irradiation; radical perineal prostatectomy was employed 3 times and 18 patients were not treated at all.

#### RESULTS OF IRRADIATION

Fifty-two patients received x-ray therapy only. The average duration of symptoms before treatment was 31.8 months. Forty-four patients were traced; 37 had died after an average of 8.19 months, and 7 were living an average of 24.5 months. Of these, 1 was well at 48 months, 5 had frequent urination but no retention, and 1 had not been benefited. The range of survival after treatment was 17 to 48 months.

Fifteen patients received radon only. The average duration of symptoms before treatment was 24 months. Thirteen were followed. Of these, 10 were dead after an average of 7.5 months, and 3 were living 35.3 months (12 to 66 months). All 3 survivors were free from symptoms.

Forty-five cases received both x-ray and radon. The average duration of symptoms before treatment was 23 months. Forty-two were traced. Of these, 34 died after an average of 14.6 months, and 8 were living 42.2 months (24 to 72 months); 2 were well; 4 had nocturia three to four times; 1 had slight straining; and 1 had not been benefited.

To summarize, 112 patients were treated by irradiation alone. Ninety-nine were followed (88.3 per cent). The average duration of symptoms was 27.2 months before treatment; 81 (81.8 per cent) were dead after an average of 10.6 months, and 18 (18.2 per cent) were living from 12 to 72 (average 34.2) months. The total duration of symptoms from onset to death was 37.8 months; the total duration of life in the survivors from the onset of symptoms to the time of checkup was 61.4 months.

#### CYSTOSTOMY

Eleven patients were treated by cystostomy. The average duration of symptoms prior to operation was 24.18 months. All were followed and all are dead. The 3 patients who received irradiation after the cystostomy lived an average of 7.78 months; the 8 who had only cystostomy survived 13.54 months. The average survival in both groups was 11.96 months. Thus, the duration of symptoms from onset to death was 36.14 months.

#### TRANSURETHRAL RESECTION

One hundred and two patients were treated by transurethral resection; the average duration of symptoms prior to operation was 33.1 months; 95 were traced.

Thirty-four of the followed cases had transurethral resection only; 2 died following operation; 22 (64.7 per cent) are dead after 13.5 months; 10 are living an average of 33.09 months. Of these, 6 are symptom free 18 to 65 months; 3 have only nocturia (16 to 73 months); and 1 has pain in the sacral region. Sixty-three of the followed cases received irradiation after resection, 13 with radon, 8 with x-ray, and 42 with both. Of these, 51 (80.9 per cent) are dead after 13.65 months, and 12 (19 per cent) are living an average of 35.09 months; 4 (6 per cent) are well 16 to 32 months; 7 have nocturia without pain or retention; and 1 is bedfast and requires morphine for pain.

The only influence of irradiation in this group seemed to be a very slight increase in longevity, and a definite reduction of the tendency to recurrent obstruction, of which there were 7 in the 34 treated by resection only, and none in the 63 who received supplementary irradiation.

To recapitulate, 97 of 102 cases treated by transurethral resection with and without irradiation were followed. Two (1.9 per cent) died after operation; 73 died after an average of 13.5 months; and 22 are living an average of 34.18 months. The total duration of symptoms was 46.5 months in those dead, and 67.28 months in those still living. Ten (10 per cent) are symptom free 16 to 65 months.

#### SUPRAPUBIC PROSTATECTOMY

Twenty-nine were treated by prostatectomy, with 3 operative deaths (10.3 per cent). All were traced. The average duration of symptoms before operation was 19 months. In 7 no other therapy was employed. All are dead after 26.6 months. Twenty-two received irradiation. Of these, 17 are dead after 23.8 months, and 5 are living 57.8 months (30 to 112 months); 4 are symptom free (36, 48, 96, and 97 months); and 1, after 112 months, requires morphine and catheterization. The total duration of symptoms from onset to death averaged 42.9 months; in those living it averages 76.9 months.

#### RADICAL PERINEAL PROSTATECTOMY

Three patients were subjected to radical perineal prostatectomy. One died of recurrence at six months. One is symptom free 91 months (best result in 275 cases); the other is incontinent of urine but otherwise well after 35 months. The cancer was discovered on physical examination for hernia in the patient living almost 8 years; symptoms had been present 4 months in the one who died; and the patient now living 35 months had had symptoms for 6 years before operation, presumably from a coexisting large benign hypertrophy.

#### UNTREATED CASES

Eighteen patients were not treated, chiefly because the disease was hopelessly extensive without causing retention of urine, but also be-



cause of absence of troublesome symptoms. Symptoms had been present for 23.95 months before the patients were first seen. Sixteen were traced; 15 had died after an average of 3.1 months; 1 was living 44 months with rather pronounced frequency of urination. The average duration of symptoms from onset to death was 27.95 months.

#### DISCUSSION

To compare the results of the various methods of treatment is difficult, both because of the small size of the various groups and because the indications for treatment were not precisely the same in all. Nevertheless, nearly all of the patients had prostatic carcinoma which had extended outside the gland itself and which had interfered with micturition. This interference was slight in the group treated by irradiation alone and severe in the others.

Four criteria of the effectiveness of treatment will be used in this discussion, namely: the mortality rate of the various groups as compared to the expected rate in the general male population at the average age (69) of the whole group; the survival after treatment; the duration of life after the onset of symptoms as compared to that of a group of untreated cases; and the numbers of symptom-free survivors.

Figs. 1 and 2 show how carcinoma affected the expected mortality. The top line in each represents the expected mortality rate in the general male population (Dublin and Lotka). The bottom line shows the mortality in 18 untreated controls, and the intermediate lines those in the various types of treatment. They were computed by adding together the deaths in each group during each successive year following treatment, converting the resultant figure to the percentage of that particular group, and starting the graph at the age of 69, which was the average age of the whole group. Thus, for the purpose of the graph, all patients who survived treatment were considered as living at the age of 69; and all deaths occurring in the first year after treatment as having occurred between the ages of 69 and 70. All of the lines, except those pertaining to cystostomy, are necessarily incomplete because there are patients still living in all other groups. It is obvious that the development of prostatic carcinoma increases the mortality rate far above that normally expected, and this without regard to the treatment employed; however, treatment retards the mortality rate very definitely when the untreated controls are considered.

On this basis the best results have followed partial suprapubic prostatectomy supplemented by irradiation, since a higher percentage of patients are living for a longer time than after any other form of treatment. However, these graphs ignore an operative mortality of 10 per cent because it is not chargeable to the disease per se; if this were included, the curve would be less favorable.

Allowance should be made for the fact that practically all of the patients receiving prostatectomy had concealed and, hence, early cancer and for the fact that the last operation in this series was done in 1932, so that more time has elapsed since treatment than in any other group. Moreover, the three radical perineal prostatectomies were included in this group because they were too few to permit the construction of a second graph.

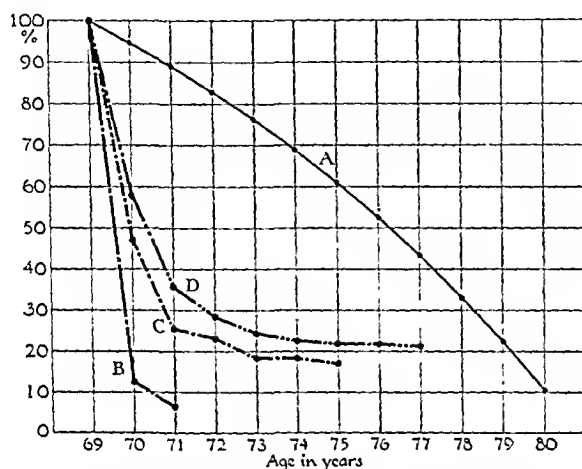


Fig. 1.—Survival after treatment for carcinoma of the prostate. A, Expected survival of male population; B, survival of untreated cases of carcinoma of the prostate; C, after irradiation; D, after all forms of treatment combined.

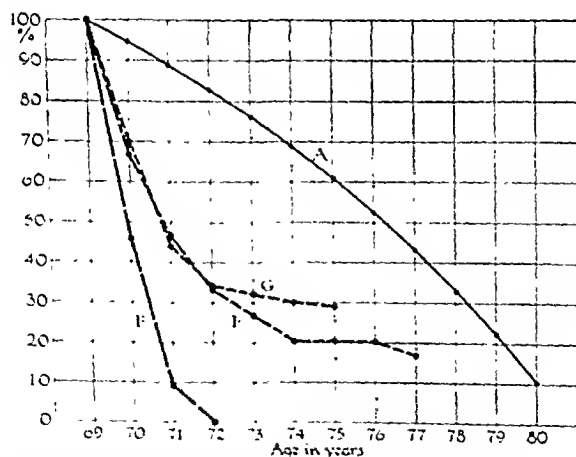


Fig. 2.—Survival after treatment for carcinoma of prostate. A, Expected survival of male population; B, survival of untreated cases of carcinoma of the prostate; C, after irradiation; D, after all forms of treatment combined; E, survival after cystostomy (with and without irradiation); F, after transurethral resection; G, after prostatectomy.

When these facts are considered, it is evident that transurethral resection is probably as effective as prostatectomy so far as longevity is concerned, and that it achieves this result at one-fifth the mortality.

When one adds the fact that the hospital stay with transurethral resection is one-third that of prostatectomy, the advantages of the former are still more apparent, except in the case of localized cancer where only radical perineal prostatectomy seems to offer any hope of cure.

There is disappointingly little difference between the results of the various types of treatment when their effect upon the total duration of the disease from the onset of symptoms to death is considered (Table I). As can be seen, this varied from 36.1 months in the case of cystostomy to 46.5 months in the case of transurethral resection (ignoring the single radical perineal prostatectomy). The differences among the various groups are probably not great enough in relation to the total duration of life to warrant consideration. This is also true of the duration of the disease in those still living which varies from a low of 61.4 months with irradiation to a high of 94 months with radical perineal prostatectomy. Even in the untreated group there was one patient surviving more than 5 years after the onset of the disease. In other words, the duration of life after the onset of

TABLE I  
RESULTS OF TREATMENT FOR CARCINOMA OF THE PROSTATE

TYPE OF TREATMENT	NUMBER OF PATIENTS	NUMBER TRACED	DURATION (MO.) BEFORE TREATMENT	DURATION AFTER TREATMENT				DURATION OF SYMPTOMS FROM ONSET (MO.)		PATIENTS SYMPTOM FREE		
				DEAD		LIVING		DEAD	LIVING	NUMBER	DURATION (MO.)	%
				NO.	MO.	NO.	MO.					
Irradiation	112	99	27.2	81	10.6	18	34.2	37.8	61.4	6	21.75	7
Resection	102	95	33.1	73	20.7	22	34.1	46.5	67.2	10	29.6	10.5
Partial prostatectomy	29	29	19.0	24	25.2	5	57.8	42.9	76.9	4	69.2	13.9
Cystostomy	11	11	24.1	11	11.9	0	-	36.1	-	0	-	0
Radical perineal prostatectomy	3	3		1	4.0	2	63	8.0	63	2	63.0	66.6
Total	257	237		190		47	38.7	42.06	66.2	22	39.8	9.3
Control series (untreated)	18	16	23.95	15	3.1	1	44	27.05	67.95	0	-	-

symptoms was but little lengthened by any form of treatment. This statement must be qualified by pointing out that both the average survival after treatment and the average survival after onset of symptoms are rendered inaccurate by the fact that many of the patients are still living and may live long enough to bring the averages of the whole group well above the stated figure. Since nearly all of the survivors are old men who still have cancer, this seems improbable.

Best results in terms of length of survival after treatment followed partial suprapubic prostatectomy with 20 per cent of those surviving

operation living an average of almost 5 years after operation. While this is exceeded by radical perineal prostatectomy (66 per cent living 63 months), the latter group is too small to permit the drawing of worth-while conclusions.

When allowance is made for the fact that more time has elapsed since treatment by prostatectomy than by resection, the results from the latter are good enough (20 per cent living 34 months) to suggest that, in the long run, they will equal those of partial prostatectomy.

None of the criteria stated above involves the question of greatest interest to the average patient; namely, the prospect of survival without symptoms. This cannot be determined accurately, of course, since dead patients cannot answer questionnaires and since it is practically impossible to secure adequate information upon this point from the relatives and local physicians of a large group of charity patients. It is, therefore, necessary to fall back upon the number of symptom-free survivors, disregarding the obvious fact that it is more comfortable to live for a year with a normally functioning bladder than to live for two while depending upon a catheter or cystostomy apparatus. On this basis there is little room for satisfaction in any of the groups.

Again, the good showing of radical perineal prostatectomy (66.6 per cent well 63 months) is spoiled by the fact that this is a group of two cases. Partial prostatectomy with irradiation has yielded 13.9 per cent of symptom-free survivors living an average of 69.2 months. This rises to 15.3 per cent if operative deaths are excluded. Transurethral resection stands third with 10 per cent well after 29.6 months, and irradiation fourth with 7 per cent after 21.75 months.

The extraordinarily poor showing of cystostomy is explained by the fact that it was employed only in those patients whose condition was too poor to permit surgical relief of the obstruction to urination, or into whose bladder the resectoscope could not be inserted.

Results in the whole group are not reassuring. Out of 275 patients with carcinoma of the prostate, 257 were treated, and 237 (92 per cent) of these were followed. Forty-seven (15.6 per cent) are living an average of 38.7 months, of which 22 (9.3 per cent of the whole group) are free of symptoms after 39.8 months. Whether any of these has actually been cured is open to question. Most of the data concerning the patients' present status are based upon answers to questionnaires; those who actually returned for examination all had evidence that cancer was present but controlled. The two possible exceptions are those who had radical perineal prostatectomy; neither has any evidence of tumor at present.

It is necessary to mention three desirable results of irradiation which cannot be brought out by these statistics; namely, the relief of pain from extension and metastasis and the distinct diminution of the

tendency to recurrent obstruction after its surgical relief. No data are available to evaluate the former, but it is very definite. The latter is demonstrated by the fact that 7 of the 35 patients treated by transurethral resection alone returned with recurrent obstruction, while none of the 67 who had resection and irradiation did so.

An additional consideration is the clinical impression that the majority of patients receiving only irradiation noticed a distinct improvement in urination.

#### SUMMARY AND CONCLUSIONS

1. The results of treatment in 275 cases of carcinoma of the prostate are reported. Of these, 253 were followed; 112 were treated by irradiation alone, 102 by transurethral resection supplemented in 67 by irradiation; 29 were treated by partial prostatectomy, 11 by cystostomy, 3 by radical perineal prostatectomy, and 18 were not treated.
2. Of the whole group, 15.6 per cent were living an average of 38.7 months and 9.3 per cent were symptom free an average of 39.8 months.
3. After radical perineal prostatectomy, 2 of 3 patients were well after 35 and 91 months.
4. After partial suprapubic prostatectomy, 4 of 26 (15.0 per cent) surviving operation are well 69.2 months.
5. After transurethral resection, 10.5 per cent of 95 patients are well 29.6 months.
6. After irradiation, 7 per cent are well 21.75 months.
7. No form of treatment has reduced the mortality per year to that for the general male population.
8. No form of treatment has influenced materially the total duration of the disease.
9. Irradiation is of value for the relief of pain, for retarding or preventing the recurrence of obstruction to urination after its surgical relief, and for the relief of low grade obstruction to urination.
10. Transurethral resection accomplishes the same result as partial prostatectomy, with one-fifth the mortality and one-third the hospital stay. It does not cure the disease, but merely relieves the obstruction.
11. Except when localized within the gland itself, cancer of the prostate cannot at present be cured.

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## THE TREATMENT OF POSTOPERATIVE PULMONARY ATELECTASIS

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IN A MOST complete review of the history of massive pulmonary collapse, Bowen<sup>1</sup> found many instances of its medical recognition during the nineteenth century. Although numerous accurate pathologic descriptions appeared and several instances of its experimental production are recorded, it was not generally accepted as a clinical entity until the Englishman, Pasteur, rediscovered the disease. His first publication on the subject appeared in 1890, to be followed in 1908 and again in 1910<sup>2</sup> by increasingly clear descriptions of atelectasis. This latter paper is generally accredited as establishing the existence of pulmonary collapse, although a much better understanding of the disease resulted from his "Annual Oration on Post-Operative Lung Complications" in 1911.<sup>3</sup>

Gairdner<sup>4</sup> in 1850 first hypothesized that a mucous plug in the bronchus would cause a collapse of the lung. He favored, however, the theory of a ball-valve action occurring at the fork of a dividing bronchus. In 1878 Liethelm<sup>5</sup> actually produced a pulmonary collapse by placing laminaria tents into the bronchi of rabbits. He was the first to show experimentally that collapse occurs as a result of absorption of the trapped gas into the pulmonary circulation. Elliott and Dingley<sup>6</sup> in 1914 reported eleven cases of atelectasis and were firm in their contention that the disease resulted from the plugging of a bronchus with mucus. Further evidence that a bronchial obstruction would cause atelectasis was presented by Jackson and Lee<sup>7</sup> in 1925. They reported a case of pulmonary collapse in a 12-year-old boy with complete relief following bronchoscopic removal of a mucous plug.

Atelectasis was produced experimentally by Lee, Ravdin, Tucker, and Pendergrass.<sup>8</sup> Mucous plugs were removed bronchoscopically from patients and placed into the bronchial trees of dogs. Under deep ether anesthesia these animals promptly coughed up the transplanted mucus. However, after suppression of the cough reflex with large doses of intraperitoneal barbiturates, the mucus was found to remain in situ and there developed a distal pulmonary collapse. Coryllos and Birnbaum<sup>9</sup> produced experimental atelectasis by plugging the bronchus of dogs with toy rubber balloons and expressed the opinion that an obstruction

of the bronchus is the only etiologic factor of importance in pulmonary collapse. When their balloons were contaminated with pneumococci, infection always developed in the atelectatic lung. Galbraith and Steinberg<sup>10</sup> placed rubber sponges into the bronchi of anesthetized dogs. Within twenty-four hours the air caught in the obstructed lung was absorbed and complete collapse developed. Careful microscopic and gross studies of the involved lung revealed increasing degrees of infection to the point of abscess formation. If, however, the sponge was removed within twenty-four hours, the lung promptly re-expanded, leaving no permanent changes.

That a mucous plug obstructing the bronchus is not the only factor in the production of atelectasis was suggested by Briscoe,<sup>11</sup> who was able to produce varying degrees of collapse in the rabbit by division of the phrenic nerves. Muller, Overholt, and Pendergrass<sup>12</sup> demonstrated the marked reduction in vital capacity following abdominal operations. They expressed the opinion that elevation of the diaphragm and restriction of respiratory movements diminished the air flow through the adjacent lobe of the lung to the point of stasis and favored collapse of the lower lobes. Churchill and McNeil<sup>13</sup> and Powers<sup>14</sup> measured the vital capacity of postoperative patients and demonstrated that a uniform reduction occurred. Webb, Forster, and Gilbert<sup>15</sup> in 1921 published an interesting observation. They placed a normal person continuously in the horizontal position on one side and found that a marked displacement of the mediastinum with opacity of the lung developed on the dependent side. When the subject was allowed to sit up and take a few deep breaths, the mediastinum immediately returned to a normal position and there was complete clearing of the lung. Galbraith and Steinberg<sup>10</sup> introduced a cannula into the right main bronchus of a dog and instituted forced respirations into this right lung only. Windows were then made in both pleural cavities, thus eliminating the negative pressure surrounding the left lung but not obstructing the bronchus. Complete atelectasis with the associated inflammatory changes in the left lung was present within twenty-four hours, during which time the dog was kept alive by forced respirations into his opposite lung. From this experiment they expressed the opinion that obstruction of the bronchus per se is not necessary for the production of atelectasis.

Another possible factor in the production of a bronchial obstruction is the aspiration of saliva during a general anesthetic. Lowenthal<sup>16</sup> performed immediate postoperative bronchoscopies on twenty-one patients reacting from an ether anesthetic. In 76 per cent of these cases saliva was recovered from the trachea and bronchi. The development of an atelectasis following a pulmonary hemorrhage has been described by Heaton.<sup>17</sup> He reviewed seven reported cases and found that in six instances re-expansion occurred spontaneously within two months. The remaining case was relieved by bronchoscopic removal of the clot.



Lander's belief that both obstructive and compression collapse occur gave rise to his classification of atelectasis as either active or passive. However, today there is general agreement that in the final analysis postoperative pulmonary atelectasis is the result of an obstructing mucous plug preventing air from passing into the distal lung and thus allowing absorption of the trapped gas.

It must be recognized that varying degrees of collapse occur: (A) involvement of a whole lung; (B) involvement of one lobe; (C) involvement of multiple patchy areas which usually occur on one side. The viscosity of the obstructing mucus varies with the size of the bronchus occluded. Thin mucus blocks only the small bronchioles and produces a patchy atelectasis; whereas, the thick heavy tenacious mucus is always present in those patients having a massive collapse.

The secondary factors contributing to the development of postoperative pulmonary atelectasis are many.

1. Pre-existing acute or chronic tracheobronchial infections: Acute exacerbations of such disorders are not unusual following a general anesthetic, shock attendant to a major surgical procedure, or simple dehydration.

2. Abdominal operations: By reducing the vital capacity and the respiratory movements, abdominal operations favor the development of atelectasis. Eliason and McLaughlin<sup>18</sup> claim that high abdominal operations are more frequently followed by collapse than operations elsewhere. However, Christopher and Shaffer,<sup>19</sup> from their series of cases, believe that low abdominal operations with trauma to the oblique abdominal wall muscles are more of a predisposing factor than upper abdominal incisions. This is explained by the fact that the internal and external oblique muscles are accessory muscles of respiration.

3. Tight abdominal dressings: Compression bandages over the abdomen tend to elevate the diaphragm, thus diminishing the capacity of the thorax with resulting lung compression.

4. Spinal anesthesia: This is thought by Brown,<sup>20</sup> Brunn,<sup>21</sup> and others to predispose definitely to the development of atelectasis because of an active depression of the respiratory center.

5. Voluntary suppression of the cough reflex: This is a common finding after abdominal operations. It definitely favors the development of a mucous plug by allowing retention of tracheobronchial secretions.

6. Morphine, barbiturates, and other sedatives: These drugs depress the cough reflex and slow respirations, thus favoring retention of mucus in the tracheobronchial tree.

7. Atropine: The dehydrating effect of atropine on the bronchial secretions has often been mentioned as a possible contributing factor. That it may be unimportant is suggested by the fact that atelectasis is just as common following operations under spinal and local anesthesia

when no atropine is given as following a general anesthetic. Beaumont<sup>22</sup> in 1935 advocated the use of atropine for treatment of the shock and collapse accompanying atelectasis.

8. Dehydration: Inspissation of thick or tenaceous tracheobronchial secretions may occur as the result of dehydration from an excessive loss of body fluids in connection with surgical procedures.

9. The position of the patient: The frequency of collapse of the dependent lung following operations necessitating a prolonged unnatural posture has been pointed out by Christopher and Shaffer,<sup>19</sup> Farris,<sup>23</sup> Scott and Joelson,<sup>24</sup> and others. Forced decubitus position definitely decreases the respiratory movement in the dependent chest, prevents adequate elimination of secretions by coughing, and favors incomplete aeration of this lung. Just as the patient with an acute appendicitis seeks a comfortable position and tends to lie on the right side with the knees and body flexed, so does the postoperative patient try to take tension off his wound by assuming a comfortable posture. While elevation in Fowler's position greatly facilitates the act of coughing, it nevertheless keeps both main bronchi dependent and thereby encourages the stagnation of mucus in the bronchial tract.

The established facts regarding postoperative pulmonary atelectasis are as follows: (1) The disease exists in several forms, depending upon the degree of collapse. There may be collapse of multiple small patches, one or two lobes, or the entire lung. Bilateral pulmonary collapse has even been described by Miller and by Sante. (2) The etiology in the final analysis is the presence of a mucous plug which blocks the main bronchus, a lobe bronchus, or a bronchiole. Contributing factors are of secondary etiologic significance. (3) The condition tends to clear spontaneously. (4) Atelectasis tends to recur. (5) Collapse gives rise to an increase in the negative pressure of the involved hemithorax with a shift of the midline structures to the affected side (Elkin<sup>25</sup> and Habliston<sup>26</sup>).

The rational treatment of postoperative pulmonary atelectasis gradually has evolved as the basic pathologic lesion has been clarified. Artificial pneumothorax to overcome the acute respiratory distress caused by mediastinal shift to the involved side has been recommended by Beaumont,<sup>22</sup> Farris,<sup>23</sup> Habliston,<sup>26</sup> Gundry<sup>27</sup> and Lander.<sup>28</sup> In 1938 Zukschwerdt and Lezin<sup>29</sup> reported a series of fourteen cases of postoperative massive collapse. In every case the production of an artificial pneumothorax was followed by the coughing up of viscid mucus with complete clearing of the involved lung within two to five days. In this country it is usually condemned as being an empirical treatment and not attacking the underlying cause. Brunn and Brill<sup>30</sup> have pointed out the inadvisability of causing a pressure readjustment by artificial measures.

Bronchoscopic aspiration of the obstructing mucous plug has been widely acclaimed as it aims at removing the etiologic agent in post-

operative pulmonary collapse. Such observers as Jackson and Lee,<sup>7</sup> Gundry,<sup>27</sup> Brunn and Brill,<sup>30</sup> Coryllos,<sup>31</sup> Hearn and Clerf,<sup>32</sup> Iglauer,<sup>33</sup> and Perrone<sup>34</sup> have stressed the positive relief that may be obtained by bronchoscopy. The obvious disadvantages of this type of treatment are, first, that bronchoscopy may be a very trying procedure when performed on a postoperative patient; second, that competent bronchoscopists are available only in the larger communities; and third, that as the disease tends to recur repeated bronchoscopy manipulations frequently are necessary. This last objection becomes more formidable when one remembers that these patients are newly postoperative, usually having had an abdominal operation.

In May, 1927, Sante<sup>35</sup> made his first report on postural drainage. While fluoroscoping a patient with postoperative pulmonary collapse, he witnessed a complete re-expansion of the lung following a sudden coughing attack which brought up a large plug of mucus. He recognized the important role played by posture in producing this result and advocated, as an effective therapeutic measure for atelectasis, that the patient be rolled back and forth with his involved side up. Some seventy-seven years earlier, in 1850, Gairdner,<sup>4</sup> in discussing bronchial obstructions wrote, "under the influence of an emetic and a forced decubitus on the opposite side to that on which the dulness existed, almost every trace of it had disappeared in thirty-six hours and the dyspnea was entirely relieved." However, to Sante goes the credit of publicizing a type of postural drainage effective in postoperative pulmonary atelectasis. One year later, 1928,<sup>36</sup> in his second article on the subject he advised that bronchoscopic aspiration be instituted when his method of relief had failed.

Scott and Cutler<sup>37</sup> reported in 1928 that postural drainage had in their hands proved ineffectual. Bowen,<sup>1</sup> Brunn and Brill,<sup>30</sup> and Lee, Tucker, and Clerf<sup>38</sup> all point out that postural drainage may be an effective method of treatment, but resort to bronchoscopy without too much delay. Postural drainage has met with a greater success in the hands of Christopher and Shaffer,<sup>19</sup> Sante,<sup>35, 36</sup> and Mathes and Holman.<sup>39</sup>

Hyperventilation of the postoperative patient by means of a mixture of carbon dioxide and oxygen has been widely practiced for a number of years. In 1906 Henderson in discussing acapnia with relation to shock first suggested that inhalations of carbon dioxide might have some beneficial therapeutic use. In 1920<sup>40</sup> he called attention to the use of postoperative inhalations of carbon dioxide and oxygen as a valuable procedure in the prophylaxis of atelectasis and pneumonia. Artificial hyperventilation has now been widely approved as being an important adjunct in both the prophylaxis and treatment of postoperative atelectasis.

On the Surgical Service of the Cincinnati General Hospital about thirty-five cases of postoperative pulmonary atelectasis are recognized every year. The reason for this high incidence is not clearly understood, but it is thought to be largely due to the prevalence of chronic respiratory infections in the patients admitted to this charity hospital. Confronted with this sizable and frequent complication, gradually there has developed a more or less routine method of treatment.

The most reliable prophylactic measures have been found to be hyper-ventilation with carbon dioxide and oxygen, breathing exercises, hourly changes in position, and adequate hydration. Abdominal binders are regularly used in the support of rectus incisions as they allow the patient to move about more freely in bed and considerably diminish the pain upon coughing. The tendency toward elevation of the diaphragms with attendant lung compression seems to be of secondary importance for, by using a binder, the patient responds more willingly to measures directed toward the elimination of bronchial secretions.

Any patient developing a sudden or unexpected elevation of the temperature or respiratory rate during the first two days after operation is suspected of having atelectasis until proved otherwise. An immediate examination is made by a member of the resident surgical staff. The common positive findings are: shrinking of the involved hemithorax with respiratory lag, a shift of the trachea toward the involved side, and the presence of coarse rhonchi heard on gentle coughing or deep breathing. If a diagnosis is established, the following procedure is carried out.

If not already in use, a tight abdominal binder is applied. The patient is changed from Fowler's position to that illustrated in the accompanying photograph (Fig. 1). The pillow is removed and the head is dropped flat, leaving the knees elevated. A chair is placed under the foot of the bed and the patient turned so that his affected side will be up. The physician then stands behind the patient and places one hand upon the uppermost shoulder rolling the patient slightly forward upon his abdomen. This puts the main bronchus in a true vertical position and secures the greatest gravitational effect on the bronchial secretions. The patient is instructed to place his uppermost hand on his abdomen, over his wound, and this is reinforced by the free hand of the physician.

Occasionally, simply placing the patient in this position initiates violent productive coughing. As a rule, however, it will be necessary to coax the patient to cough. In the majority of cases the plug will be loosened by the first guarded cough and an uncontrollable cough reflex set up with the production of a sizable quantity of mucus. Coughing is encouraged until rhonchi no longer can be felt by the palpating hand. It is not uncommon for such a patient to volunteer the information,

"that's all." If this fails, or if the patient absolutely refuses to cough because of incisional pain, there are several other tricks to be tried. Further efforts are aimed at loosening the plug. If this can be accomplished, a fit of coughing will follow regardless of whether the patient attempts to suppress it or not. With this in mind, he is asked to take a few deep breaths. Failing to produce the plug a sharp blow on the back frequently will accomplish the desired result.

There will be an occasional case in which all of the above maneuvers fail. In this event, with the patient still in the correct position, carbon dioxide inhalations are given to increase the depth of respirations and, as pointed out by Perrone,<sup>34</sup> this will not infrequently loosen the plug.



Fig. 1.—The knees are elevated and the foot of the bed raised on a chair. The abdominal binder, patient's hand, and the hand of the physician all reinforce the abdominal incision. The physician's other hand keeps the patient rolled toward his abdomen. This hand also detects the clearing of rhonchi as the mucus is coughed up.

If rhonchi still persist and breath sounds are not coming through the involved lung, the patient is forced to remain in the described position for as long as one-half hour at a time. During this period a steam inhalation of tincture of benzoin is given using an ordinary paper bag attached to a croup kettle. Two things are accomplished. The steam thins out the mucus, and the gravitational effect is enhanced by being allowed to act over a period of time.

This regime is only infrequently used in its entirety as the obstructing mucous plug ordinarily can be produced by simple forced coughing with the patient in the correct posture. Hyperventilation with carbon

dioxide and the use of the croup tent are reserved for those cases in which the usual methods have failed. There has been a marked uniformity of success in relieving postoperative atelectasis by the above described type of postural drainage. The most common cause of failure has been found to lie not with the method, but with its application. It might be well to point out that one of the most common errors noted in this clinic is the failure to drop the patient out of Fowler's position even though he will be turned with his affected side up. This does not alter the dependency of the large bronchi and as a result the effect of gravity is working in the wrong direction.

As no special equipment is needed, the patient may be treated immediately upon recognition of the collapse regardless of the hour of the day or night and as often as is thought desirable thereafter. The most striking relief has been noted to occur in those cases in which the atelectasis is recognized within an hour or two after onset. The longer a lung or lobe is allowed to remain collapsed, the more difficult will be its relief by postural drainage. Coryllos<sup>9</sup> states that atelectasis is merely the forerunner of pneumonia and that, if virulent organisms are present in the obstructed bronchus, some degree of pneumonitis invariably must follow. However, clinical experience supports the contention that early re-expansion of an atelectatic lobe is followed by the prompt return to normal state. Jennings<sup>11</sup> has shown, in one case, that an associated tubular bronchiectasis occurring as a result of atelectasis will clear completely with the passage of time.

This treatment was taken as a matter of course until during the spring of 1938 the resident on the Ear, Nose and Throat Service became interested in securing more cases for bronchoscopy. He inquired as to why there were no cases of postoperative atelectasis on the Surgical Service and was told that the complication occurred frequently, but was invariably relieved by conservative measures. His inquiry led to a careful study of six consecutive cases occurring between April 22 and June 18. It is not customary to take emergency portable x-ray films on these patients as postural drainage is always employed immediately upon recognition of the complication. It is considered of more importance to relieve the atelectasis promptly than to lose the forty-five minutes or one hour necessary to take and develop a portable film. Arrangements were made with the Department of Roentgenology to secure rush portable films during the daytime only. For this reason only three of these six cases were checked by roentgenograms. The remaining three presented physical signs of such clarity that a positive diagnosis could be made.

#### REPORT OF CASES

CASE 1.—M. M., No. 93317. This colored male, 31 years of age, was admitted to the Surgical Service of the Cincinnati General Hospital on April 21, 1938. A per-

forated duodenal ulcer was closed shortly after admission, using spinal anesthesia. Forty-four hours after his operation there developed a collapse of the right lower lobe of the lung. Several postural drainages produced a number of mucous plugs with a complete clearing of the abnormal physical signs within forty-eight hours.

Pyrexia and respiratory difficulty again developed three days after the first episode and a recurrence of the collapse was demonstrated by physical signs. Postural drainage was again effective in eliminating the obstructing mucous plug. His convalescence from this time on was both afebrile and uneventful.

CASE 2.—F. K., No. 93749. This 34-year-old white male was admitted to the Surgical Service of the Cincinnati General Hospital for the repair of an inguinal hernia. Although he gave a history of having had pneumonia ten times, the physical

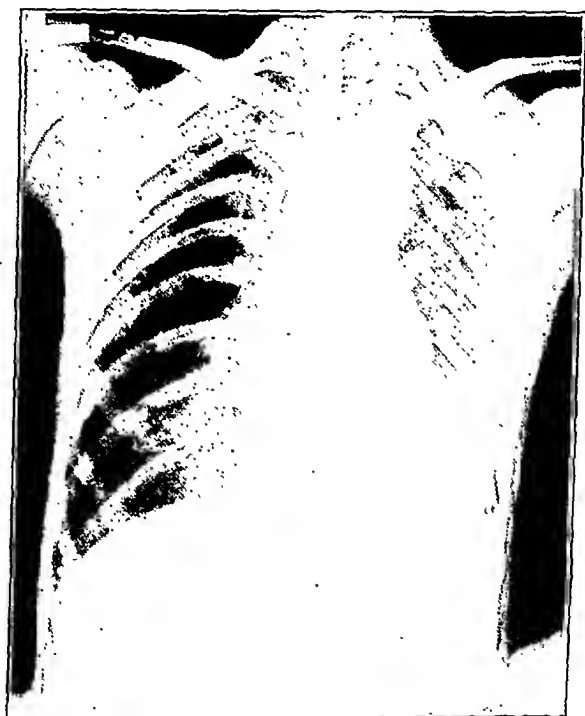


Fig. 2.—There are noted a shifting of the trachea and heart toward the left, narrowing of the interspaces on the left, and a diffuse haziness of the left base (Case 2).

and roentgenologic findings in the chest were normal. A left-sided simple hernioplasty was performed on May 3, 1938, using local field block anesthesia. Twenty-two hours after operation his temperature was  $102.4^{\circ}$ , pulse 100, and respirations 30 per minute. Telephone instructions were given to leave the patient strictly alone until he could be examined. When seen, he was found to be curled up in bed in low Fowler's position, and lying on his left or operative side. He was coughing feebly and guardedly but was producing no sputum. With every cough rhonchi were clearly audible at some little distance from the bed. He was found to have a diminution of the respiratory movement on the left side with an apparent shrinking of the left chest. There was also a marked deviation of the trachea to the left. A portable x-ray film (Fig. 2) was taken and postural drainage was then instituted. Several

large mucous plugs were obtained and the patient was encouraged to continue coughing until rhonchi no longer could be felt. Fifteen minutes after the first x-ray examination a second film was made (Fig. 3). At this time the collapse was found to have been largely relieved, the respiratory excursions were equal, and the trachea had shifted back to the midline. A second and lesser collapse occurred twenty-four hours later and was promptly relieved by postural drainage. His subsequent course was uneventful and he was discharged from the hospital fifteen days after operation.

CASE 3.—J. M., No. 93966. This white male, 48 years of age, was operated upon for a right inguinal hernia on May 13, 1938. Local field block anesthesia was used. The day following operation he was coughing up thick tenacious mucus, but otherwise was comfortable. Forty-four hours after operation his condition was quite satisfactory, having a temperature of 99.4°, pulse 84, and respirations 18 per minute.

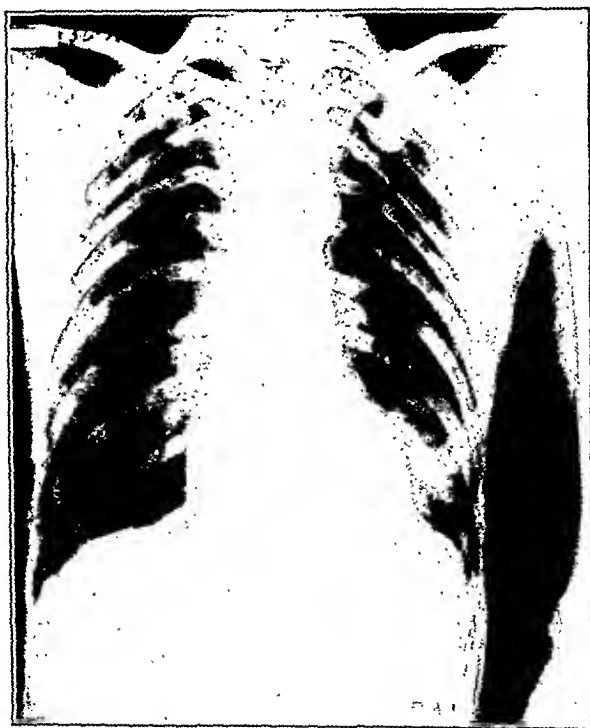


Fig. 3.—This film was taken fifteen minutes later than the film shown in Fig. 2. The trachea is back in the midline and the right border of the heart is now visible. The left base has expanded.

Four hours later his temperature was 102.4° F., pulse 120, and respirations 28 per minute. When examined his trachea was found to be shifted to the right side and the breath sounds did not come through at the right base. Postural drainage produced one large and several small batches of thick yellowish-green tenacious mucus. Following this his trachea was found to be back in the midline, expansion was equal, and normal breath sounds were heard over both bases. Twenty-four hours later his temperature was 99° F. and during his subsequent convalescence did not go above 99.2° F.



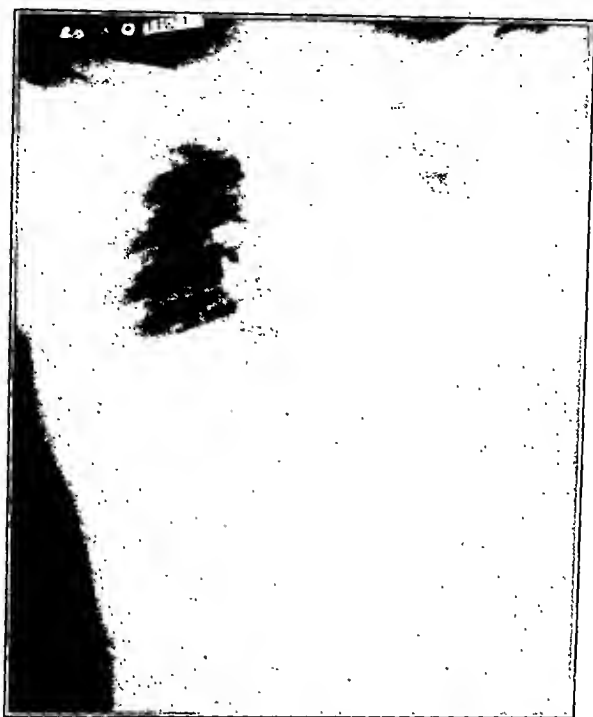


Fig. 4.—The left base is airless and collapsed (Case 4).



Fig. 5.—This film was taken twelve hours later than the film shown in Fig. 4. There is very little residual haziness in the left base; however, the diaphragm is still slightly elevated.

CASE 4.—O. F., No. 94647. This patient, a white female, aged 27 years, was admitted to the Surgical Service of the Cincinnati General Hospital on May 23, 1938, with a diagnosis of exophthalmic goiter. Following nine days of preparation, a sub-total thyroidectomy was performed under local anesthesia. Thirty-two hours after operation her temperature of 101.8° F. and pulse rate of 120 per minute were not considered unusual. However, within a four-hour period her respirations jumped from 22 to 38 per minute. She was found to have coarse râles scattered through both lungs, but no definite evidence of pulmonary collapse could be discovered on physical examination. The following morning there was discovered an atelectasis of the left lower lobe. A portable x-ray film corroborated the diagnosis and also revealed a shift of the trachea which it had been impossible to detect clinically because of the thyroidectomy (Fig. 4). Postural drainage afforded prompt relief with complete re-expansion as shown by another film taken twelve hours later (Fig. 5). An x-ray film made twenty-four hours later revealed no residual pathologic findings (Fig. 6). The patient was discharged from the hospital eight days after operation.



Fig. 6.—After another twenty-four hours, it is noted that complete re-expansion has occurred (Case 4).

CASE 5.—H. E., No. 96506. This 55-year-old white male was operated upon for a left inguinal hernia on June 15, 1938. Local field block anesthesia was used. Twenty-four hours after operation his temperature suddenly rose to 102.6° F., pulse to 116 per minute, and respirations to 30 per minute. Examination revealed a collapse of the left lower lobe as demonstrated by a respiratory lag, a shifted trachea, and alteration of the breath sounds at the left base. As his case occurred during the daytime, an x-ray examination was requested, but it was found that due to technical difficulties there would be some delay. Rather than allow the collapse to remain over this period, postural drainage was instituted and the patient coughed up several plugs of tenacious yellowish mucus. His signs of atelectasis cleared promptly; however, he continued to produce small quantities of sputum during the ensuing



Fig. 7.—This portable film shows complete collapse of the left lung (Case 6). That portion of the duodenal tube that lies in the upper esophagus is seen shifted far to the left side.

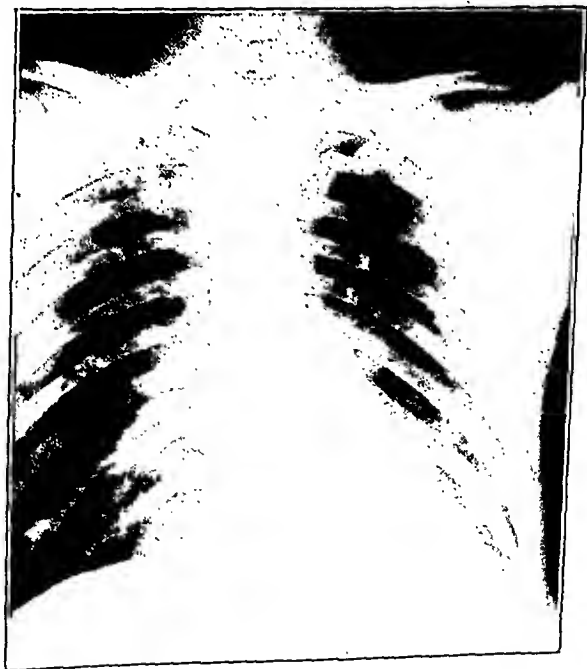


Fig. 8.—Six days after the massive collapse, there is complete aeration of the left lung (Case 6).

week. His temperature spiked at a lower level for the next three days, after which time it remained normal. He was discharged from the hospital on schedule.

CASE 6.—E. R., No. 96648. This patient, a white male, 26 years of age, was admitted to the Surgical Service of the Cincinnati General Hospital on June 17, 1938, because of a ruptured gastric ulcer. Simple closure of the perforation was performed under spinal anesthesia. Twenty-six hours after operation his temperature was 102.4° F., pulse 108, and respirations 40 per minute. As the medical consultant was suspicious of pneumonia, an attempt was made to type the sputum, but no pneumococci were found even after injection into a mouse. A portable x-ray film (Fig. 7) established the diagnosis of massive collapse of the left lung. The indwelling Wangenstein tube nicely demonstrated the shift of the mediastinal structures toward the involved side. Postural drainage produced many plugs of thick tenacious mucus, but it was impossible to clear completely his lungs of rhonchi at any one time. Repeated efforts to bring up the mucus were successful as shown by an x-ray film (Fig. 8) taken six days after the collapse occurred. His convalescence was otherwise uneventful.

#### COMMENT

Since atropine was not given to any of these patients, it could not have been a factor in the development of atelectasis.

Periodic postoperative hyperventilation with carbon dioxide and oxygen was administered to two of these patients (both ruptured peptic ulcer operated upon under spinal anesthesia). This procedure failed to prevent the development of atelectasis. That this experience has not been unusual at this clinic may be due to the fact that the method used here is not entirely adequate.

As the remaining four patients were operated upon under local anesthesia, no prophylaxis against pulmonary collapse was used. Postural drainage, as described, effectively relieved the collapse in each of these patients in sequence. In two instances there was a recurrence of the atelectasis, but a prompt response was obtained by a repetition of the same therapy.

#### SUMMARY

Postoperative pulmonary atelectasis results from the occlusion of a bronchus by a mucous plug. Factors contributing to the development of such a plug are: pre-existing tracheobronchial infections, recumbency, dehydration, and suppression of the cough reflex both as a voluntary act following abdominal operations and as a result of sedative drugs. The efficacy of the method of postural drainage used at this clinic for relieving atelectasis is well illustrated by the six cases here presented.

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## ARTERIAL INJECTIONS WITH STASIS IN THE THERAPY OF INFECTIONS\*

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THE possible usefulness of arteriotherapy was suggested to us by the first arteriogram that we made and immediately afterwards it was applied to certain diseases not only through the arteries of the extremities but also by the aortic and carotid routes. In studying the history of arteriotherapy, it was found that Goyanes,<sup>1</sup> in 1914, first used this method in tuberculous arthritis. Although soon afterwards it was abandoned, nevertheless it is of historical importance. The method was used also by Leriche,<sup>2</sup> in 1913, and by Heddaus,<sup>3</sup> in 1914, and consisted of injecting antitetanic serum by the carotid route. We believe, however, that we are the first to utilize intra-arterial therapy extensively and to apply it by another route; that is, through the abdominal aorta. In 1929 at a conference held in Leriche's clinic in Strasbourg the principles and my observations and results were presented.<sup>4</sup> More extensive investigations were published subsequently by my assistants and myself.<sup>5-10</sup> Whereas Leriche has expressed the opinion that in his experience the value of the procedure has not been found sufficiently convincing, the difficulty of demonstrating the superiority of a method applied to infections diverse in character, localization, and severity, particularly where other methods are also beneficial, is well known. The comparative value of results is of significance only when they are controlled, because it is difficult to deduce the results of therapy based solely upon the clinical impression. Even statistics may not suffice, as in this instance in which the series is too small. One is forced, therefore, to resort to personal experience.

In infections of the extremities arterial injections have been tried in Italy, especially by Lucearelli.<sup>11</sup> In Austria, Demel and Sgalitzer<sup>12</sup> employed abrodil intra-arterially for arthritis. Therapeutic arterial injections have been used most extensively by the French. A review of these observations will reveal that, in general, these investigators consider the procedure valuable.<sup>13-20</sup>

The carotid route has been used by a number of investigators. In 1929 E. Moniz<sup>21</sup> observed the therapeutic effect of sodium iodide injected into the carotid artery in cranial hypertension. Leriche,<sup>2</sup> Heddaus,<sup>3</sup> Fritzsche,<sup>22</sup> and Fourmestraux<sup>23</sup> injected antitetanic serum by the carotid route. Fritzsche employed this method in fifteen severe cases with only

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two deaths. His observation in a case of generalized tetanus, in which at first an injection in the left carotid only had been made, is particularly demonstrative. Whereas the convulsions were bilateral, following the injection they almost disappeared on the right side but scarcely diminished on the left. This demonstrates the significance of the therapeutic action on the cerebral hemisphere corresponding to the carotid injected. The opposite side had received antitoxin only by way of the general circulation.

One of my students, Silveira Ramos, of Angola, has cured a very severe case of malignant malaria by bilateral carotid injections of quinine bromide.<sup>24</sup> Up to 1933, together with other colonial physicians, he has treated 100 similar cases with complete recovery.

In posttraumatic meningoencephalitis we have utilized successfully the carotid route since February, 1929.<sup>4</sup> After publishing our first case, it was later learned that this procedure had been used in America. The experimental investigations of Kolmer, Rule, and Madden<sup>25, 26</sup> using aeriflavine, a colloidal solution of iodine, gentian violet, and metaphen, were followed by their clinical application.<sup>27</sup> The first cases of pneumococic, staphylococic, meningococic, and streptococic meningitis successfully treated in this manner were reported by McMahon,<sup>28</sup> Crawford,<sup>29</sup> Kolmer,<sup>27</sup> and Ersner and Mendell<sup>30</sup> respectively. Finally I desire to call attention to personally observed cases of osteomyelitis of the maxilla and severe infections of the face successfully treated by external carotid artery injections of antiseptics.

The aortic route, however, remains the least employed except by us, apparently because puncture of the aorta is feared, which in our experience is not justified. Thus, all abdominopelvic infections (puerperal or postabortal), peritonitis (appendiceal, perforative, or adnexal), and all ruptures or visceral wounds have been benefited in our experience by this most concentrated, direct, and least toxic method of injecting antiseptics. In my service and in some of the emergency services this is routine. The cases operated upon receive the injections at the end of the operation. The dorsal route is always used because it is simpler and less dangerous than puncture through the open abdomen. The dorsal route of aortic injection may be employed also in blood transfusion, either because venipuncture is difficult or to avoid shock by the venous route.

However, in this presentation I wish to emphasize particularly the most recent modification in technique, especially as applied to the extremities; namely, *intra-arterial injection with stasis*. The principles, as previously stated in 1929 at the conference in Strasbourg,<sup>4</sup> were: "An elastic compression suddenly applied and slowly released can retard the passage of medicaments into the general circulation and can hold them in the tissues. Radiographic proof of this fixation has been obtained in studying a series of arteriograms of the forearm with elastic



compression. Bier similarly observed this phenomenon by using intravenous anesthesia. At first the arterial shadow is visible for about fifteen minutes, then as the vessel loses its opacity the tissues gradually become more accentuated, obviously due to the fixation of sodium iodide in the tissues."

In spite of these well-established principles, because of its simplicity, for a long time we have performed almost exclusively the arterial injections into the free circulation. However, during the past year, one of my assistants, John dos Santos, studied the problem more intensively. By retaining an active solution in the tissue for a few moments, it is possible to increase its activity and thus reduce the dosage. This has been demonstrated by arterial analgesia. We have observed that novocain injected into the femoral artery in the free circulation produces no regional anesthesia and may produce either a toxic effect or even a rapid general anesthesia. On the other hand, a similar injection with stasis produces an anesthesia of the extremity which is not followed by any toxic manifestations. The tourniquet is removed slowly a few minutes afterwards. The anesthetic agent becomes fixed in the tissues and consequently enters the general circulation very slowly just as in local analgesia. This observation, as well as our serial arteriograms with stasis, explains the action of an antiseptic injected intra-arterially. Thus, with stasis the regional activity of the material injected is increased several times, the dosage can be diminished, and the general toxicity avoided. These facts, which form the basis of the venous analgesia of Bier and the arterial analgesia of Goyanes, contain therapeutic possibilities which have not been utilized.

In arteriography, despite the practice of Kroetz, we prefer the free circulation to obtain the anatomic and functional characteristics of the circulation, but in arterial therapy the problem is different. It is not a question of determining the functional activity which has a diagnostic significance, but of obtaining an action as concentrated, as profound, and as prolonged as possible, without injury either to the tissues or to the vessels.

The following technique has been described by my assistant, John dos Santos: A short, fine needle (0.8 mm. in caliber and 3 cm. in length) with a short point is connected to a rubber tube which in turn is attached to a syringe. Injection through a diseased area should be avoided. The compression is made over healthy tissue above the lesion. In lesions of the proximal or midportion of an extremity it is preferable to use two tourniquets. The distal tourniquet is tightened before the injection; the other, the sphygmomanometric cuff placed proximal to the lesion, is inflated only after the end of the injection. The brachial or femoral artery is then punctured. The application of the tourniquet above or below the puncture is of little or no importance. Facility determines the site of the puncture.

In infections of the hand and forearm puncture of the brachial is performed at the elbow and the tourniquet is applied to the forearm or arm, according to the site of the lesion; but in infections above the elbow it is necessary to inject brachial or the exposed axillary. The avoidance of this difficulty will be discussed later. In the lower extremity the puncture is simple as all regions are accessible for injection without exposing the artery and the tourniquets limiting the diseased zone retain the solution in the desired area.

In performing the injection, it is desirable to have two assistants. In the author's service usually two nurses perform this function. One assistant pumps air into the sphygmomanometer at the desired moment. The other assistant holds the syringe ready to inject the solution. The syringe and the rubber tube are filled with the antiseptic solution. Mercurochrome and 1 per cent acriflavine are the agents most commonly used. The distal tourniquet is tightened until the peripheral pulse has disappeared. The proximal tourniquet, i.e., the sphygmomanometric cuff, is applied to the extremity over healthy tissue and above the lesion. The artery is then punctured and a small red, pulsating stream of blood coming from the needle indicates accuracy of arterial puncture. The rubber tube is then attached to the needle. The assistant injects the solution in the syringe; as soon as this is finished the other assistant pumps up the sphygmomanometer to 300 mm. of mercury. Before removing the needle from the artery, the rubber tube is disconnected from the needle to see if blood still spurts, thus assuring accuracy of injection. Circulatory stasis is maintained for ten to fifteen minutes.

*Comment.*—The injection at first is not painful, but approximately two minutes after stasis has been produced pain may be experienced and apparently is commensurable to the concentration or quantity of solution fixed in the tissues. Whereas in most cases it can be tolerated, it is desirable, if it is very intense, to administer a general anesthetic. As soon as the tourniquet is removed, the pain disappears. The use of an isotonic solution, as Huet<sup>19</sup> has suggested, should be considered.

Disappearance of pain and decrease in inflammation are the first signs of improvement. The skin reaction is quite distinctive and is characterized by a vasomotor response and a discoloration. In peripheral arterial disease it is very interesting to observe the permeable area of the skin, which becomes red or blue upon injecting mercurochrome or methylene blue, respectively, according to the degree of circulatory involvement. This is a direct Moszkowicz test and therefore has a diagnostic application. Vasomotor phenomena, such as attacks of arterial or venous spasm, occur more frequently in the upper extremity, but this is readily relieved by novacain block of the stellate ganglion. Such attacks have always been stopped by this method and arterial thrombosis has never occurred. The absence of a general reaction is proof that arterial injections with stasis are without danger, particularly because it is possible

to diminish the dosage. John dos Santos has observed that the general feeling of warmth produced by intravenous injection of calcium gluconate remains localized if this method of stasis is used, and, even when the tourniquet is removed, it does not appear. The febrile reactions which occur regularly following intravascular injections without stasis do not develop if stasis is produced. Since this technique has been used, it is our firm conviction that the results are certainly better and superior to the previously employed arterial injections without stasis. The procedure has been applied particularly to the following conditions: (1) Infections of the soft parts, phlegmon, deep abscesses, and especially infections of the hand and foot; (2) acute and subacute osteomyelitis; (3) compound fractures either prophylactically or therapeutically in combating infection; (4) articular infections.

Twenty cases have been treated by this method and its superiority is shown by the rapidity with which the infectious process has been controlled. In some cases this has occurred within twenty-four hours. Disappearance of pain, limitation of diffuse processes, lowering of temperature, and diminution of leucocytosis further characterize its remarkable action. In the majority of cases drainage becomes unnecessary which is particularly important in the forearm, the hand, or the foot. Of considerable comparative value is a case of osteomyelitis of both tibiae, in which we applied arterial injection with stasis only to the worse side. Whereas the infection was promptly controlled on this side, the opposite side drained for a long time.

Only three observations of John dos Santos will be reviewed briefly:

CASE 1.—Male, 50 years of age, admitted as an emergency with a phlegmon of the forearm and immediately treated by arteriotherapy with stasis. Tourniquet was applied to the midportion of the arm, and 10 c.c. of 1 per cent mercurochrome were injected into the brachial artery at the elbow. Stasis was maintained for ten minutes. As the phlegmon involved the entire forearm, six small incisions, 2 cm. in length, were made in the upper portion. There was no drainage. Two days later the patient was fever free and practically no suppuration occurred, but as a precaution another injection with stasis was made. The next day there was no evidence of suppuration and eight days later the wound had healed with the exception of superficial cicatrization.

CASE 2.—Male, 22 years of age, who fifteen days previously had injured the midportion of the right hand with a bone. Upon admission a very severe infection of the entire right hand was observed. The general condition was very bad, with marked weakness and some delirium. The entire hand and forearm appeared edematous, indurated, and very tender. The fingers were in semiflexion. There was no sign of fluctuation and the leucocyte count was 15,000. Intra-arterial injection of mercurochrome with stasis was done. The next morning practically all the pain had disappeared, the temperature dropped to 37.5° C. and the leucocytosis had decreased to 11,000. That evening the temperature went up to 38° C. and another injection was performed. The next day there was no more pain and the temperature was 37° C. That evening it was only 37.5° C. Finally, on the third day he was fever-free both morning and evening. However, superficial fluctuation was beginning to appear in the forearm and in order to prevent extension of the infection a third

injection was made with stasis. The next day the leucocyte count was 8,800 and a very small localized purulent collection (staphylococci and a few streptococci organisms were found) was drained. Following this the wound healed very rapidly. Thus, it may be stated that a very diffuse infection was transformed into an almost aseptic localized suppurative process without fever and without pain.

CASE 3.—Female, 36 years of age, admitted with a phlegmon of the entire forearm which followed an infection of a small wound over the elbow. There was marked edema of the hand and the temperature was 39° C. An intra-arterial injection was made and six minutes of stasis maintained. The pain diminished shortly afterward and the patient was able to sleep. The next day there was limitation of the suppurative process and it was incised and drained. The following day the pain, fever, and edema had disappeared. Six days later the wound had practically healed. This case was less severe than the preceding one as one injection sufficed. However, in the more severe cases it is possible to give the injections once every twenty-four hours and even twice in the same day.

In considering the treatment of infections by a regional, prolonged action of an antiseptic solution in the tissues, it should be realized that this can be accomplished by the venous as well as by the arterial routes. It is possible to obtain regional anesthesia by two methods, that of Bier and that of Goyanes, as has been stated previously. Just as these two surgeons attempted to obtain an anesthetic effect by novocain fixation in the tissues after producing circulatory stasis, we have tried to obtain a therapeutic effect by fixing an antiseptic solution in the tissues also by stasis. Therefore, the stasis is an essential factor. However, it is necessary to consider which is the more preferable route, the arterial or the venous.

At present our experience with the arterial route is more extensive. We have made comparative studies of the two routes which we will present later, but from the physiologic standpoint it seems to us that, in general, the arterial route is preferable: first, because it assures a better distribution of the antiseptic solution in the tissues; and second, because by the use of a tourniquet it permits the solution to be retained in the desired region. Moreover, since it is merely a question of simple puncture, the injection can be performed easily and as often as is necessary. Since in the lower extremity the injection is always made in the groin, the dosage must be slightly increased for infections of the foot and lower leg because of the dilution when it arrives in this distal region. In this area the venous route is probably easier to apply. The injection is made into the internal saphenous below the tourniquet on the leg in the opposite direction of the circulation. In this way the entire foot can be reached, but the solution must be considerably diluted (1 part to 1,000), and the quantity sufficiently great (50 to 100 c.c.). For the thigh, the intravenous method is less favorable (as is the intravenous anesthesia of Bier), because a large dosage of the solution is necessary to fill the venous system up to the capillaries. Thus, the arterial route is preferable for the thigh and the knee; the venous route, easier for the

foot. In the upper extremity the arterial route is certainly better for infections of the forearm and the hand, the puncture being made at the elbow. The venous route perhaps would be better indicated for the arm as the exposure of an artery, which is necessary, would be more difficult than that of a vein.

Finally, if the tourniquet cannot be placed above the lesion, is it still possible to produce the effect of stasis? Yes, this can be accomplished to a less complete degree by compression of the artery after the injection. Thus, the subclavian or the carotid arteries are exposed through a small incision and compression is applied immediately after the injection. Even in aortic injections as a complement to laparotomy (appendicitis, peritonitis following gastrointestinal perforation) it is possible before closing the abdomen to make an injection in the aorta by the dorsal route, which is always easier, and to compress the aorta against the vertebral column for a few moments while the abdomen is still opened.

These directions and principles of the technique are based upon an experience which, up to the present, includes more than 300 cases. Whereas the former type of arterial injection has already made great progress in the treatment of infections, the present method with stasis is considered vastly superior and has the advantage of permitting the use of a less concentrated and a decreased amount of solution.

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# GRAVITY DRAINAGE OF INFLAMMATORY EDEMA

## A METHOD FOR ELEVATION OF AN EXTREMITY

JAMES KNOTT, M.D., CHRISTIANSTED, VIRGIN ISLANDS

**I**N AN editorial in this JOURNAL, Waagensteen<sup>1</sup> has discussed the role of immobilization and posture in the treatment of acute infections of the extremities. He concludes as follows: "Clinical trial suggests that immobilization and elevation are adjunct measures of distinct value in supporting the natural defense mechanism of the body in pyogenic infections of the extremities. Their use appears to rest on a rational physiologic basis."

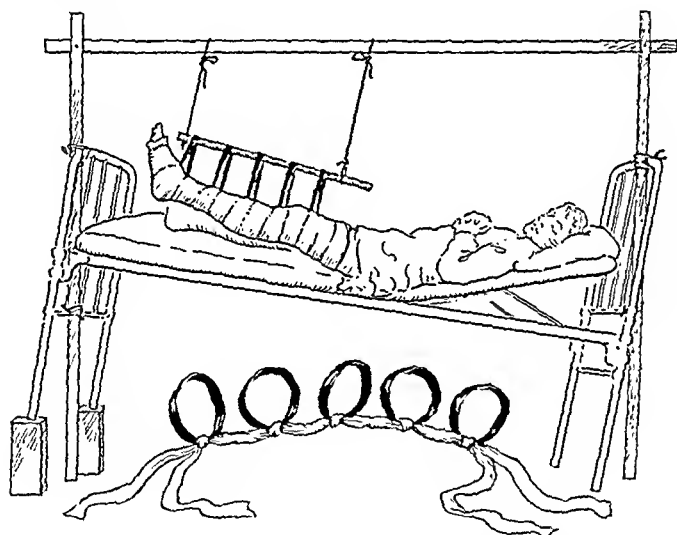


Fig. 1.—The foot of the bed is elevated on 10-inch blocks and the limb hangs suspended from the broomstick passing through the rubber rings. Insert shows method of fastening rings together.

I have had two years' experience with a method of elevation which has pleased me very much. The extremity hangs suspended at the desired elevation. The patient can move the limb and can change his position in bed without pain, and without disarranging the elevation.

The foot of the bed is put up on 10-inch blocks. The wound is dressed and the limb wrapped with 6 inch wide strips of bath toweling from the toes to mid thigh. A large sterile bath towel, folded lengthwise, is laid along the under surface of the limb. Five rubber rings, made by cutting cross sections from an automobile inner tube, are tied together.

One end is attached to the foot over the ankle and the other end above the knee. A snug bandage is applied, incorporating the rubber rings. A broomstick, hanging from an overhead frame, is passed through the rings and the leg suspended.

The arm can be suspended in a similar fashion but the elbow and wrist should be splinted on the under surface.

In acute infections which have not yet localized, the dressings should be changed daily and the limb gently inspected for abscess localization, which would require incision.

Limbs with plaster casts can be suspended with comfort to the patient. I have also used the method in terminal care of carcinoma of the breast with elephantiasis of the arm.

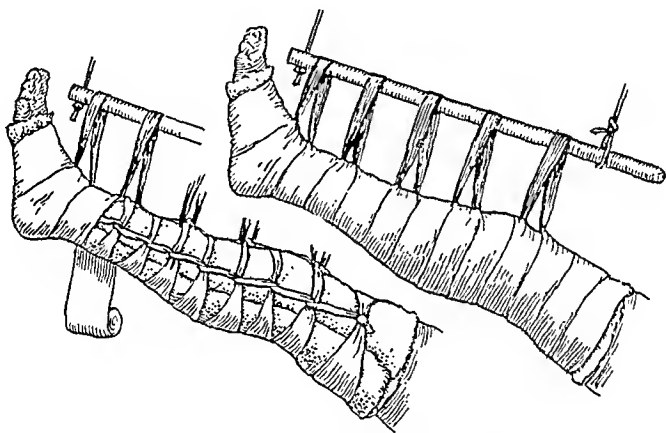


Fig. 2.—Showing method of attaching the rubber rings to the limb with bandages. Note that bowline loop in end of rope permits broomstick to be slipped out without untying.

The method was originally developed for the preoperative removal of lymphedema in elephantiasis of the leg. The patient can slip out the broomstick, walk to the bathroom, and on return replace the leg as it was. After Kondoleon operation, the limb is kept suspended until wound healing is complete.

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# Editorial

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## The Responsibility of the Surgeon for Postoperative Complications

**M**ODERN SURGERY began when anesthesia and asepsis had become established. Before this time the pain of the ordeal or the almost inevitable sepsis which followed every operation restricted surgical therapy to a few serious and painful conditions. It was only natural that what we now look upon as postoperative complications and not a part of the original disease should have been lost sight of in the terror of the ordeal itself.

With the advent of modern surgery arose the field of elective surgery, for now it was possible to remove painlessly and with safety diseased organs from patients otherwise in good health. But again surgery was shown to be a mixed blessing. Just as when in the days following the discovery of anesthesia postoperative sepsis halted all surgical advance, so now serious and often fatal complications were noticed even in "clean" cases where the wound healed per primam. Patients died of pulmonary complications, and coma, anuria, and tetany followed certain procedures. From this time to the present an unremitting study of the causes of such complications has gone forward. Slowly but surely the surgeon has learned the risks of surgical therapy, and he now understands the incalculable benefits of proper preparation of his patient. Careful studies have revealed that certain disorders, which now can be appreciated by simple biochemical tests, will give rise to serious complications unless they are adjusted preceding the surgical procedure. Other studies have made it clear that the frequency and severity of pulmonary complications vary with the site of the operation and the type of technical surgery practiced.

These studies have given rise to the conscientious attitude of the modern surgeon whose energies are directed quite as much to a complete appraisal of the general condition of his patient and to measures calculated to improve the "risk" as to the treatment of the condition from which the patient suffers. To begin with, a more reasonable preparation of the patient arose through a better appreciation of the chemical and physiologic changes that occurred when surgery was attempted. Forty years ago it was the rule to starve, purge, and withhold water as preoperative routine. Now we have learned that perhaps the best preparation is that one which disturbs the patient as little as possible from his normal ways of diet, of exercise, and of living. Moreover, surgeons have noted that the patient hurriedly brought from an active life to the operating table because of trauma or intra-abdominal acute dis-

order, as with rupture of a duodenal ulcer, is not likely to have serious postoperative complications. To emphasize this point we have only to consider the seriously toxic thyroid patient. Every surgeon who does thyroid surgery takes care lest his patient be disturbed the morning of the operation. On the other hand, if we happen to have a healthy young boy with a hernia, he is often awakened early, his teeth given a special scrubbing, he is given a bath and sometimes an enema—a considerable ordeal to the unpracticed—all before he goes to the operating room. It is obvious that we still have to untie ourselves from many customs imposed by a preceding generation of surgical thinking!

When we consider postoperative sequelae we can say that much has been accomplished. There is both experimental and statistical evidence that the various pulmonary complications occur under all forms of anesthesia, including infiltration anesthesia and spinal anesthesia. From this we may broadly deduce that the anesthetic per se is not the essential responsible factor which gives rise to these unfortunate pulmonary complications. And yet one hears constant criticism of anesthetists and anesthetics. Furthermore when infectious lesions spread or when new infection is introduced at the operation, there is a constant tendency to speak of the diminished resistance of the patient or to blame the catgut or to say that the house staff suffered from "colds."

It has long appeared that this point of view has the unfortunate and serious aspect that it represents an attempt of the surgeon to search outside of the patient for the cause of the sequelae. Obviously no single factor extraneous to the patient is present in every case. The temperature of the operating rooms, the kind of anesthesia, "colds" among the assistants, and the type of surgery are all variable conditions. But we have in the wound itself, made by the surgeon, a single, always present source of trouble! It is obvious that in every surgical operation thrombi form where vessels are cut. These thrombi may be larger in those cases where there is unnecessary trauma, where tissues are roughly handled, and where desiccation is allowed to occur. Such thrombi are more apt to be of large size if vessels have been clamped and the ties put on distal to the clamped area so that injured intima and slowed circulation, chief factors in thrombosis, are present. Such thrombi, if they slip off, produce infarction with inevitable peripheral morbidity.

Every surgeon of experience appreciates the grave danger of surgery in certain infectious lesions, as, for example, carbuncles about the lip. Why is it that the lessons learned in this field cannot be applied elsewhere? In the surgical care of infection, whether it be a furuncle, a subcecal appendix, or an abscess of the brain or of the lung, the same desiderata are called for; that is, that the opening be made in the part nearest to the lesion so that a minimum of uninvolved tissue will be cut. When the lesion is superficial, the opening should be made in the center of the inflamed area so that the walling-off process which nature throws

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# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## HEPARIN: A REVIEW OF ITS HISTORY, CHEMISTRY, PHYSIOLOGY AND CLINICAL APPLICATIONS

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### INTRODUCTION

DURING the past few years rapid progress has been made in the problem of preparing heparin suitable for clinical use. This substance now can be purified to such a degree that it may be introduced into man without fear of any untoward effects other than those which may arise consequent upon rendering the circulating blood incoagulable. At present pure heparin is a relatively expensive product, a factor which may retard considerably developments in its therapeutic application; however, the recent advances in knowledge of its chemical structure offer the hope that in the near future heparin itself, or equally active and useful synthetic compounds of similar structure, will become available at more moderate costs.

The clinical possibilities of a nontoxic anticoagulant are numerous, and a considerable literature on this subject has arisen. It has seemed well, therefore, to attempt to summarize some of the existing information concerning heparin from several points of view. It is the purpose of this review to discuss briefly its history, chemistry, mechanism of action, and recent physiologic and clinical investigations involving its use.

### HISTORY

The first recorded observations of the anticoagulant properties of heparin were those made by McLean<sup>1</sup> in Howell's laboratory while studying the thromboplastic behavior of several phosphatides. Two were found to inhibit clotting: *cuorin*, prepared from heart muscle by the method of Erlandsen,<sup>2</sup> and the *heparphosphatid* of Baskoff,<sup>3</sup> isolated from dog liver. Shortly afterward Howell and Holt<sup>4</sup> made an extensive study of heparphosphatid. They observed that although the *cuorin* prepared by McLean was identical with that of Erlandsen, the *heparphosphatid* he had isolated differed somewhat in its properties and nitrogen-phosphorus ratio from the original preparation of Baskoff.

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about each infection may protect the patient from a spreading process. Think how often the scalpel is swept across an infected area and then out into a fresh and heretofore uncontaminated and therefore unprotected field! And consider this in relation to the common operation of appendectomy. It is unhappily the habit of some surgeons to utilize the same incision always for appendectomy. If a right rectus incision is always employed, the abdominal cavity will be opened in a certain number of people who have retrocecal appendicitis with abscess, and the abscess may be broken into from the side of the free and heretofore uninfected peritoneal cavity in order to secure drainage. This means contamination of the abdominal cavity; whereas, a posterior, muscle-splitting incision in the flank would have avoided opening the abdominal cavity. It is unfortunate that the lessons learned in the bacteriologic laboratory are not more intimately applied in the clinic!

When we consider the occurrence of new wound infection, we must consider the suture material, or the dry goods that come out of our autoclaves, or finally the treatment of the tissues themselves. In the first place, catgut and kangaroo tendon material can never be considered absolutely aseptic. In the next place the autoclaves in every hospital must be constantly and scrupulously checked for adequate performance. The surgeon cannot delegate this responsibility entirely to the nurse or the hospital administration. If he himself has insufficient knowledge of how to do this, he should call in experts to assist him. Finally we must accept the fact that every wound receives contamination from the skin and air bacteria. The deeper layers of the skin cannot be sterilized. The circulating air always contains bacteria, though they can be somewhat reduced by the expensive process of washing the air and perhaps by the use of infrared rays in the operating room. The question is, can the body care for the number of bacteria which inevitably will be introduced? This we know will depend upon what has gone on in the wound. If the tissues have been allowed to dry, if there has been rough handling so that many cells are dead or are dying, if great tabs of tissue have been strangulated by gross ligature material so that they have lost their blood supply and are to undergo necrosis, the few bacteria introduced may cause dissolution of the wound, breaking down of the healing process, and suppuration.

All of the considerations above should direct the attention of the surgeon to the fact that the one thing common to every operation is the wound. If his technical performance is carried out with gentleness and with high regard for the life of each individual cell, then at least some of the unfortunate postoperative sequelae will disappear.

—*Elliott C. Cutler, M.D.*

Boston, Mass.

place heparin could no longer be demonstrated in plasma. Its normal anticoagulating influence was presumed to be neutralized by cephalin liberated in shed blood.<sup>7</sup>

Shortly following the isolation of crude heparin by Howell and Holt, the firm of Hynson, Westcott, and Dunning (Baltimore) undertook its production for general physiologic use. The preparations since available from several American and European firms have had potencies (purities) ranging from that of crude heparin to the 1925 product of Howell. Only very recently has the chemically pure substance been obtainable, in consequence of the investigations of Schmidt and Fischer, Charles and Scott, Bergström, and Jorpes, whose work will be considered in the section dealing with the chemistry of heparin.

Studies of the mechanism of action, physiologic and chemical properties, and possible clinical application of heparin paralleled progress in its purification. These will be discussed in appropriate sections subsequently.

#### MECHANISM OF HEPARIN ACTION

The controversies over the mechanisms involved in blood coagulation which have arisen in the past forty years are outside the scope of this review and have been dealt with adequately elsewhere.<sup>9-17</sup> It may be stated unequivocally that the problem has not been solved nor are any of the prevalent theories consistent with all experimentally confirmed facts. Only a portion of that literature directly concerned with the behavior of heparin will be considered.

Inasmuch as heparin is intimately concerned with the Howell theory, it is convenient to discuss it from that standpoint. The Howell hypothesis may be briefly stated as follows:

There are present in circulating blood prothrombin, calcium ions, fibrinogen, antithrombin, antiprothrombin (heparin) and an antithrombin precursor (proantithrombin). The antiprothrombin (heparin) has the function (1) of stabilizing prothrombin by combination with it, and (2) of promoting the production of antithrombin from its precursor, proantithrombin. (At any rate the latter action is claimed for heparin *added* to plasma.)

In shed blood, thromboplastic substance (cephalin) liberated from injured tissues or platelets combines with antiprothrombin (heparin). The unstable prothrombin reacts with calcium ions forming thrombin, which, when in excess of the antithrombin, permits the conversion of fibrinogen to fibrin.

Explicit functions, therefore, are assigned to heparin. These are (1) that it acts as an antiprothrombin and (2) that it stimulates the production of antithrombin by activation of a precursor (proantithrombin<sup>4,7</sup>). Implicit to this theory is the presence of heparin in blood as a physiologic constituent, necessary for the maintenance of its fluidity.

For the heparphosphatid with which they were dealing, Howell and Holt proposed the name "heparin" to indicate its origin in liver, and they described in detail the procedure they used in its preparation free from cephalin. The acetone precipitate of the ether soluble fraction of dried dog liver was repeatedly precipitated from alcohol at 50° C. until it began to lose its solubility in anhydrous ether. It was then taken up in chloroform and precipitated twice from warm alcohol. The final product when dried and pulverized was a chocolate powder, water soluble, heat stable, and had a nitrogen-phosphorus ratio of 2.5:1. One hundred milligrams per 100 c.c. shed blood completely inhibited clotting, and intravenous injections of 100 mg. per kilogram into dogs greatly increased the clotting time of subsequently drawn blood. The effect wore off in three to four hours. No changes were observed in blood pressure, heart rate, respiratory rhythm, or rectal temperature in these experiments, nor in those of Reed.<sup>5</sup> From experimental evidence it was concluded that heparin had two effects upon the coagulating system: (1) it inhibited the activation of prothrombin to thrombin by calcium, by reacting in some way with prothrombin; and (2) it was an activator for "proantithrombin" permitting the conversion of this postulated substance into antithrombin. While admitting there was no direct evidence that heparin occurs normally in blood, these authors believed the indirect evidence favored the hypothesis that both heparin and proantithrombin are physiologic constituents.

In 1923 Howell<sup>6</sup> published an alternative method of preparation that yielded a more active crude product, which was further purified<sup>7</sup> by employing taka diastase to destroy accompanying glycogen, boiling, methyl alcohol to precipitate any protein, and cadmium chloride to eliminate other undefined contaminants. One gram of crude heparin yielded 18 to 20 mg. of the purer substance, 1 mg. of which prevented the coagulation of 40 c.c. of cat blood. Further purification<sup>8</sup> was obtained by precipitation as the barium salt, which when freed of barium and dried was an almost colorless, sealy material, water soluble and heat stable, 1 mg. sufficing to keep 100 c.c. of blood liquid. The absence of phosphorus in this preparation forced the conclusion that the active substance was not a phosphatide, and that previous positive tests for this element were due to contaminants. The reactions of this purer heparin in the blood coagulation system were the same as those of crude heparin.

Using the action on proantithrombin and the anticoagulating activity as tests, heparin was demonstrated in (1) the plasma of dogs in peptone shock (moderate quantities) and (2) normal dog plasma (minute quantities). In establishing anticoagulating activity of the plasma, the contained heparin was concentrated by a brief procedure consonant with obtaining crude heparin. After clotting had taken

It is difficult to reconcile with the work of Clowes<sup>31</sup> the assumption that cephalin (thromboplastic substance, tissue extract, platelets) liberates prothrombin by entering into chemical or physical combination with the stabilizing heparin. This investigator added cephalin to citrated plasma, passed the mixture through a Berkefeld filter which retained the lipoid, and then found the filtrate did not promptly coagulate upon recalcification unless additional cephalin was added.

Directly opposing the implications of this observation are the investigations of Fischer<sup>32, 33</sup> which indicate (1) that thromboplastic material rapidly removes heparin from solution and (2) that this reaction is a stoichiometric one forming a dissociable complex.

Not a few investigators, e.g., Eagle,<sup>34</sup> indicate that a case can be made for heparin being an artificial substance produced by tissue manipulation, and that the isolated product may in no way be related to the physiologically circulating anticoagulant, if, indeed, there be such. This appears extreme in view of the facts which will be considered in discussing its chemistry. It would seem that in light of the existing differences of opinion, a temporarily safe position regarding the role of heparin might be stated as follows.

Heparin is probably, but not certainly, the normal circulating anticoagulant assisting in or necessary to the maintenance of the fluid state of the blood. Its anticoagulant action is effected largely through its power to activate a precursor to antithrombin rather than by any combination with prothrombin which renders the latter insensitive to thromboplastic substance and calcium ions. Although under certain conditions heparin and thromboplastic substance may enter into combination to "neutralize" one another, the coagulating activity of the latter is largely due to the increase in thrombin caused by its action on prothrombin.

It is realized that such a conception is entirely unsatisfactory and represents merely one point of view that may be gained from the literature on this vexed subject. The unhappy state of the problem of the nature and action of the physiologic anticoagulant is emphasized by the excellent discussions of Eagle.<sup>34, 35</sup>

#### THE CHEMISTRY OF HEPARIN

The literature on the chemistry of heparin may be divided into two categories: that dealing with (1) its isolation, identification, and probable structure, and (2) its chemical properties in vitro. For convenience the first category will be dealt with chronologically.

*The Isolation, Identification, and Probable Structure of Heparin.*—The early observations on the chemical properties of heparin were made by Howell who followed his isolation of crude heparin<sup>4</sup> by further purification<sup>6, 7</sup> and finally prepared a product with an activity of 100 units per milligram.<sup>8</sup> (For comparison, "pure" heparin is now conceded



The double action of heparin seemed well substantiated by the original observations of Howell. In addition prothrombin is now believed by many to be identical with complement "mittel-stuck,"<sup>18</sup> and heparin has an inhibitory action on this component of complement.<sup>18, 19</sup> The claim for its occurrence as a physiologic constituent of blood has been supported by several lines of evidence: (1) It is a substance which can be isolated from a number of tissues other than liver and lung;<sup>20-22</sup> (2) by similar methods of isolation, a substance with identical properties may be isolated (a) from normal plasma in minute quantities, and (b) from the incoagulable plasma of the peptonized dog in larger amounts, but (c) none is to be obtained from the serum of clotted blood;<sup>7</sup> (3) protamine forms an insoluble inactive complex with heparin in vitro, and also effectively diminishes clotting time of shed blood either by addition in vitro or by previous intravenous administration;<sup>23, 24</sup> (4) mucoproteins, containing mucioitinsulfuric acid, have a wide physiologic distribution and are particularly rich in the Ehrlich mast cells in areolar connective tissue,<sup>21, 22</sup> the granules of which contain mucioitinpolysulfuric ester, i.e., heparin (vide infra).

In spite of the attractiveness of the Howell concept of heparin function, there is considerable evidence against it. The assumption, by practically all investigators interested in heparin from points of view other than its mechanism of action, that it functions as an antiprothrombin is not justified at the present time. Mellanby<sup>25</sup> and Quick<sup>26-28</sup> have made it appear more than likely that heparin does not act as an antiprothrombin but exclusively as an antithrombin (Mellanby) or as an activator to an antithrombin precursor which is albumin (Quick). The latter prepared purified prothrombin by Eagle's method<sup>29</sup> and showed that upon addition of calcium chloride, thrombin was formed readily and in the same amounts in the presence or absence of added heparin. Also heparin was found not to inhibit the action of thrombin on fibrinogen which had been isolated by sodium chloride precipitation, thus refuting Mellanby and strengthening part of Howell's earlier interpretation that addition of heparin produced an antithrombin from some precursor. Finally, it was shown that the coagulation time of oxalated plasma as well as purified fibrinogen is inversely proportional to the concentration of thrombin, a straight line relationship which would not hold if appreciable amounts of antithrombin were present, and which is disturbed by the addition of minute amounts of heparin. This is interpreted as indicative of the absence of antithrombin, and, accordingly, heparin in normal blood.

Against the conception that heparin enters into combination with prothrombin is the observation that certain proteolytic enzymes change prothrombin to thrombin,<sup>30</sup> although here it may be possible that these enzymes split off heparin as well as directly attack prothrombin.

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an activity of approximately 500 Howell cat units\* per milligram, the insoluble brucine salt fraction being somewhat higher (vide infra). The following observations were made by Howell on this product: phosphorus and nitrogen, negative; no reduction of Fehling's solution until after hydrolysis; no color with iodine (glycogen test);  $\alpha$ -naphthol reaction (Molisch) positive; test for glycuronic acid (Tollen's naphthoresorcinol and Bial's orcinol reagents) positive; hydrolysis with dilute hydrochloric acid destroyed its anticoagulant activity giving a water soluble residue behaving like glycuronic acid; boiling with dilute nitric acid, and evaporation left a sticky residue mixed with an inorganic crystalline deposit containing calcium and sulfur; ash, 37 per cent.

It was concluded that heparin was probably a glycuronic acid derivative or condensation product containing, as isolated, calcium and sulfuric acid in the molecule. In support of this it was found that glycuronic acid heated to  $250^{\circ}$  formed a dark-colored water soluble condensation product which had an anticoagulating activity of one to two units per milligram.

In 1933 Schmitz and Fischer,<sup>36</sup> starting with a Kahlbaum preparation of heparin, succeeded in preparing a crystalline brucine salt which had thirty-two times the anticoagulant activity of the original material. The method of assay had been previously described by them,<sup>37</sup> and cannot be compared directly to that of Howell; however, it may be presumed, in light of later developments, that this product had the same order of activity as pure heparin, which, indeed, it seems to have been except, probably, for a small amount of ash resulting from the binding of cations by the acidic groups.<sup>38</sup> After removal of phosphate by magnesia mixture, they adsorbed the active material on silica gel, and after elution, prepared two lead salts, one of which contained the active substance. After removal of the lead, a barium salt was precipitated from which, in turn, a brucine derivative was made. The formula assigned to the free acid was  $C_{18}H_{32}O_{17} \cdot 6H_2O$ . Incinerating the barium salt in sulfuric acid yielded only traces of ash other than barium sulfate, but neither the free acid nor the brucine salt was entirely ash-free, and they ascribed this to the ability of heparin to bind salts, stating that the ash content, hence the composition of heparin, changes with the mode of preparation. In their opinion pure heparin should be considered ash-free.

In a subsequent paper<sup>39</sup> they stated that heparin is probably a carbohydrate compound with a molecular weight of about 650, containing one free carboxyl group. The Molisch and naphthoresorcinol tests were positive, but there was no reducing activity until after acid hydrolysis, which suggested the presence of an uronic acid with a

\*A Howell cat unit is that degree of anticoagulant activity required to inhibit clotting of 1 c.c. of cold cat's blood for twenty-four hours.

blocked aldehyde group. No nitrogen was reported, but the high barium content of the barium salt was remarked upon. It was thought this was due to salt binding power rather than to heparin acting simply as an anion.

Almost simultaneously, the findings of Charles and Scott appeared in three important papers. The first<sup>40</sup> dealt with the large scale preparation of crude heparin from beef liver. For details of this procedure, which differs considerably from Howell's, the original description should be consulted. The second<sup>20</sup> concerned the distribution of heparin in various tissues determined by the quantities which could be extracted from them. In the ox it was found that liver, muscle, and lung yielded comparable amounts, the latter tissue being richest. Much smaller quantities were obtained from heart, thymus, spleen, and blood. Only negligible amounts were recovered from serum. Dog liver contained about twice as much as that of the ox. The third paper<sup>41</sup> dealt with the purification of crude heparin. Upon a preliminary, partially purified product several important observations were made. It contained 3.2 per cent nitrogen and the activity was destroyed by treatment with nitrous acid, indicating that heparin contained a free amino group which was concerned in its anticoagulant action. It was stable to oxidizing and reducing agents. In alcohol the ammonium salt was soluble, whereas the sodium salt was insoluble, suggesting the formation of definite salts, and the presence of a carboxyl group.

The purification of crude heparin involved considerable manipulation (see original) including removal of inactive material by Lloyd's reagent, cadmium chloride, hydrogen peroxide, and fractional precipitation with sodium chloride and acetone, during which calcium found present was removed by oxalate. Three products were prepared: (1) free heparin, (2) the sodium salt, and (3) the hydrochloride, the latter being microcrystalline, and by analysis found to be 22 per cent carbon, 37 per cent hydrogen, 27 per cent nitrogen, and 33.3 per cent ash. The other two products had nearly the same composition. The ash was stated to consist mainly of sodium chloride. The Molisch test was positive and the iodine test for glycogen negative. Contrary to Howell and Schmitz and Fiseher, the orcinol, phloroglucinol and naphthoresoreinol tests were negative even in 4 per cent concentrations. The activity of the three preparations was 421, 484, and 471 Howell cat units respectively, with an average of 459. The details of the method of assay were given.

It is seen, therefore, that at this time (1933) there was no general agreement as to either the chemical properties or composition of purified heparin. The first communication of Jorpes<sup>42</sup> did much to clarify this subject. After preparation of crude heparin according to the method of Charles and Scott, followed by partial purification by treat-

an activity of approximately 500 Howell cat units\* per milligram, the insoluble brucine salt fraction being somewhat higher (vide infra). The following observations were made by Howell on this product: phosphorus and nitrogen, negative; no reduction of Fehling's solution until after hydrolysis; no color with iodine (glycogen test);  $\alpha$ -naphthol reaction (Molisch) positive; test for glycuronic acid (Tollen's naphthoresorcinol and Bial's orcinol reagents) positive; hydrolysis with dilute hydrochloric acid destroyed its anticoagulant activity giving a water soluble residue behaving like glycuronic acid; boiling with dilute nitric acid, and evaporation left a sticky residue mixed with an inorganic crystalline deposit containing calcium and sulfur; ash, 37 per cent.

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cat units per milligram; however it is likely the actual activity at this stage was about half this value.<sup>43</sup> The naphthoresorcinol test was negative, in confirmation of Charles and Scott, but differences in technique may have explained the opposite findings of Howell, and Schmitz and Fischer.<sup>38</sup>

It would appear, then, that Jorpes was dealing with essentially the same substance which had been prepared by Schmitz and Fischer and by Charles and Scott, and which was the active ingredient of Howell's best product. The latter workers had not fully appreciated the significance of the ash content and in addition Schmitz and Fischer had failed to observe the presence of nitrogen. Jorpes' quantitative observations on ester sulfates, hexuronic acid, glycuronic acid, and N-acetyl definitely pointed to the class of compounds with which heparin must be identified and did much to explain the discrepancies other investigators had encountered in respect to the ash. (It is to be remembered that a free ester sulfuric acid would yield no ash, whereas any metallic salt of such a compound would give an ash composed of the corresponding sulfate. In the preparation of purified heparin the procedures entailed offered the possibility of the formation of metallic salts in every instance, some of which were not fully resolved by further treatment, e.g., in preparation of the hydrochloride or the brucine salt.) It was concluded that the organic material in heparin is chondroitin, and that the active anticoagulant is a chondroitinpoly-sulfuric acid or a mixture of these acids.

Schmitz<sup>44</sup> doubted this to be the case stating in a brief communication that he had prepared an extremely active heparin with an ash content of about 5 per cent, containing no sulfuric acid. Not doubting Jorpes' actual observations, he suggested that either a series of anticoagulants occur in tissues, or that derivatives of the active compound are formed during manipulation, this explaining various divergent results. Details of the testing for presence of sulfate were not given, and it is difficult to escape the conclusion that its apparent absence was an error of observation. The status of the heparin problem at this time was summarized by Jorpes.<sup>45</sup>

In a later paper Charles and Scott<sup>43</sup> report further efforts to isolate heparin in a pure form. By preparing lung heparin as the calcium salt, they were able to remove the calcium with oxalate, and reduce the ash content to 5 per cent. Then taking advantage of the fact that benzidine forms an amorphous precipitate with heparin, this derivative was prepared which, freed of benzidine and recrystallized from ether and glacial acetic acid, yielded a product with only 0.7 per cent ash. From this the barium salt was readily prepared in a crystalline form. The ash in this amounted to 33.5 per cent, the total sulfur in the crystals being 9.3 per cent and the amino nitrogen 0.4 per cent. The barium could be removed by several reprecipitations with benzidine.

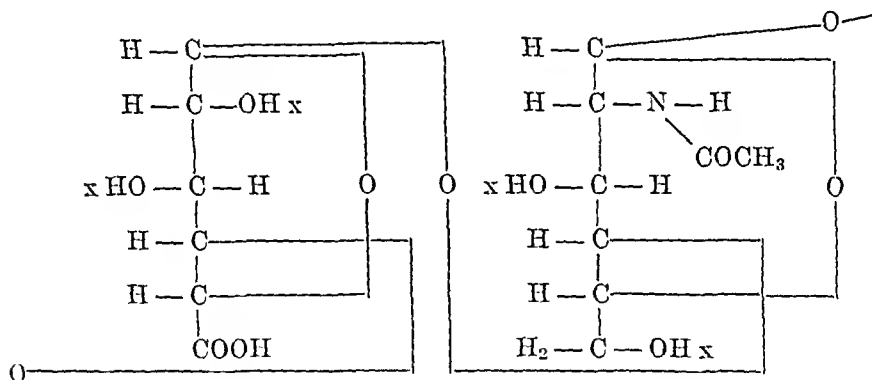
ments with Lloyd's reagent, he subjected the samples to analysis. The ash varied from 38 to 41 per cent, and nitrogen from 1.6 to 1.8 per cent. Quantitative estimation of hexuronic acid indicated 17 to 19 per cent was present, and another analysis for hexosamine yielded 12 to 14 per cent. A test for ester sulfate was positive as was that for N-acetyl. This analysis was so completely in agreement with what might be anticipated for chondroitinsulfuric acid that it seemed unlikely it could be anything else; however, chondroitinsulfuric acid was devoid of antieoagulating activity. The ash content was more carefully investigated, and about 7.5 per cent sulfur as ester sulfate was shown by electro dialysis. As chondroitinsulfuric acid contains only about 3 per cent sulfur, and as there were reasons to believe the extra ester sulfate was fixed to the chondroitin, the presumption of a chondroitin polysulfuric acid seemed plausible. The observed ratio of ester sulfate to chondroitin by analysis was about 2.5:1 which could be explained by the presence of a mixture of chondroitin trisulfuric and chondroitin disulfuric acids in about equimolecular proportions.

Study of the properties of heparin and chondroitinsulfuric acid revealed certain important differences. The barium salt of heparin readily flocculates whereas that of chondroitinsulfuric acid is soluble; likewise heparin but not chondroitinsulfuric acid is flocculated in cold methyl alcohol by brucine. Freed from brucine this precipitate analyzed as calculated for chondroitin trisulfuric acid. In addition the quinine salt was prepared from a neutral solution of heparin and after removal of the quinine, the residue had a composition agreeing with chondroitin trisulfuric acid. Finally, in order to obtain a pure brucine salt, the metallic cations of the heparin samples as well as traces of free sulfates, were removed by electro dialysis and the brucine salt precipitated in methyl alcohol. This salt had the composition approximating chondroitin trisulfuric acid, whereas the material recovered from the mother liquor contained sulfur in proportions somewhat below that calculated for chondroitin disulfuric acid.

The observation was also made that the acetic acid recoverable from heparin diminished in the final products. As these preparations maintained their antieoagulating activity it was believed the acetyl group had been split during manipulation, and that it was unessential to the antieoagulant effect. The probable importance of the ester sulfate grouping was emphasized by pointing out that almost all substances known to inhibit blood clotting effectively are high molecular weight sulfonic or sulfuric acid derivatives (liquoid, germanin, pontamine pink, chlorazol sky blue, and numerous other dyes).

The assays of the presumed chondroitin trisulfuric acid were made by a method which cannot be directly compared with that of Charles and Scott, except in two instances where the partially purified heparin prior to precipitation with brucine was assayed at about 500 Howell

clusion that heparin is to be considered a mucopolysulfuric ester.<sup>52, 38</sup> The chemistry of chondroitinsulfuric and mucopolysulfuric acids is briefly outlined by Harrow and Sherwin.<sup>53</sup> These substances are the prosthetic groups of the corresponding chondro- and mucoproteins. They consist of units of an hexuronic acid, presumably glycuronic, an amino sugar, sulfuric and acetic acids. The acetic acid is present as an N-acetyl group on the amino sugar, and sulfuric acid, one or more moles, is bound by an ester linkage to the free hydroxyl groups of the hexuronic acid and/or the hexosamine, the latter being galactosamine in chondroitinsulfuric acid and glucosamine in mucopolysulfuric acid. Removal of the sulfuric acid from these compounds yields chondroitin and mucitin, respectively. These units are probably bound to one another through the usual carbohydrate ether linkages to form chains, thus yielding a substituted polysaccharide analogous to glycogen, starch, cellulose, chitin, etc. The structure of a unit of mucitin is shown in the accompanying structural formula,<sup>52, 54</sup> the points where esterification with sulfuric acid may take place being designated by  $x$ .



Jorpes and Bergström<sup>52</sup> studied the hydrolysis rates of heparin and chondroitinsulfuric acid. It was found that the heparin prepared from the insoluble brucine salt showed a much slower hydrolysis rate than that of the soluble brucine salt, the rate of the latter approaching that of chondroitinsulfuric acid. The most highly esterified heparin is, therefore, most stable. Liver and lung heparin were found to be identical except that the proportion of highly esterified heparin in the latter is smaller, and the anticoagulating activity correspondingly lower. The amino sugar of lung heparin was also found to be glucosamine.

It was noted that the amino group in the purest heparin samples is not free, yielding no nitrogen with nitrous acid. Although the evidence is good that it is blocked by an acetyl group, only about half of the theoretical acetic acid could be recovered by measures instituted for its isolation. The hexuronate appears to be glycuronic acid, but saccharic acid was not demonstrated upon oxidation. They concluded



Calculations from analyses of the benzidine derivative gave the following composition for benzidine-free heparin: calcium, 23.1 per cent; hydrogen, 4.99 per cent; nitrogen, 2.1 per cent; sulfur, 11.54 per cent. The empirical formula assigned was  $C_{35}H_{65}O_{50}N_2S_5$ . This analysis did not support Jorpes' view that heparin is chondroitinpolysulfuric acid, the carbon content being much too low. The crystalline barium salt was inactivated by nitrous acid, formaldehyde, and prolonged exposure to acid alcohol which split off the ester sulfate groups. Its anticoagulant activity was found to be approximately 500 Howell cat units per milligram.

The work of Jorpes led Bergström<sup>46</sup> to investigate the heparin activity of several synthetic sulfuric acid esters of carbohydrates which he prepared by sulfonation. Glucose- and galactose-tetrasulfuric acids, and glucosamine-trisulfuric acid were inactive as were the esters of the corresponding polymers if hydrolyzed during sulfonation; however, the esters of the polysaccharides, cellulose, starch, glycogen, chitin, pectin, gum arabic, and chondroitin, had various degrees of anticoagulant activity. Chitindisulfuric, cellulose-trisulfuric, and pectin-polysulfuric acids were about one-tenth as active as Jorpes' purified presumed chondroitintrisulfuric acid, and the rest, other than synthetic chondroitintrisulfuric acid, were considerably weaker. The synthetic chondroitintrisulfuric acid had only about a fifth the activity of Jorpes' isolated product, a considerable discrepancy considering that by analysis the synthetic compound had between three and four moles of sulfate per mole chondroitin. It was nontoxic to rabbits, in contrast to the cellulose derivative.

The findings of Bergström were confirmed and extended by Chargaff et al.<sup>47, 48</sup> who found that anticoagulant activity was exhibited by polyvinylsulfuric acid, cellulosemono- and disulfuric acids, galactansulfuric acid and cerebroside sulfuric acids. None of these approached the activity of a partially purified heparin preparation, and they also observed a number of sulfuric and sulfonic derivatives which were inactive in spite of rather high molecular weight. They concluded that the following properties are necessary for inhibitor activity—water solubility, high molecular weight, and combined sulfuric acid, or perhaps other acids of similar strength. It is now evident that this generalization must be abandoned in favor of some more fundamental concept of the effect of charge, molecular weight, and chemical composition on the stability of proteins, e.g., Herrmann<sup>49</sup> finds certain basic dyes are strong anticoagulants. Similar observations have been made by others<sup>50</sup> employing simpler organic bases.

Recently Jorpes and Bergström<sup>51</sup> were able to show that the amino sugar in purified heparin is glucosamine, not galactosamine. The latter is characteristic for chondroitin, whereas the former is a component of the closely related mucitin, a circumstance which forced the con-

In a subsequent paper by Jorpes, Holmgren, and Wilander<sup>22</sup> the occurrence of mast cells and heparin in the blood vessel walls was further studied. Diffuse metachromasia was found in the walls of the great vessels, mast cells being especially rich in the vena cava, which might explain the delay in post-mortem clotting in it. The yields of heparin by extraction corresponded to the numbers of mast cells in these vessels. Large numbers of mast cells were found in the cornea and it was suggested that this might account for the absence of clotting when small hemorrhages occur in this region. The more general aspects of these findings, as well as a brief summary of some other phases of the physiology of heparin, were given in later communications by Jorpes.<sup>54, 59</sup>

In summary, then, it may be stated that the chief contentions of Jorpes and his co-workers regarding the chemistry of heparin appear to be correct. These may be briefly recapitulated as follows:

Heparin is not a definite chemical compound, but a mucoitinpolysulfuric ester of variable composition. The variables are (1) the number of sulfuric acid groups substituted into the individual mucoitin units, and (2) the positions into which they are substituted; (3) the degree of polymerization, i.e., the number of mucoitin sulfuric acid units which are linked together to form the polysaccharide structure, and (4) the relative esterification of each of the units so employed. The heparin preparations separated by chemical procedures have anti-coagulant activities roughly proportional to the degree of esterification with sulfuric acid, the higher esters being the most active. The insoluble brucine derivative of heparin is composed largely of the higher esters, particularly mucoitintrisulfuric ester, and has an activity somewhat greater than 500 Howell cat units per milligram. Products isolated from various tissues may differ in activity due to differences in degree of esterification, and of polymerization until the chemical fractionation affords a separation of the identical components. Heparin is found in a large number of body tissues and is concentrated in the mast cells of Ehrlich where it may be identified by the metachromatic staining reaction with toluidine blue. The anatomic locations of these cells, in connective tissue around and in blood vessels, and their staining characteristics support the hypothesis that one of their functions is the elaboration and secretion of the physiologic anticoagulant.

For the moment we must consider as "pure heparin" any mixture of the various naturally occurring mucoitinpolysulfuric esters which have been freed of extraneous materials such as protein, accompanying salts, etc. It is seen that several of the products isolated by the various investigators mentioned above satisfy these criteria.

*Chemical Properties of Heparin in Vitro.*—The strong electronegative charge of heparin makes it an agent capable of exerting considerable influence on colloidal systems. Thus, Fischer<sup>60</sup> has shown that when

that heparin was not a definite compound but a mucopolysulfuric ester containing at least the trisulfuric and probably the mono- and disulfuric derivatives. The proportions of these determine the anticoagulant activity, the greater activity being associated with the higher sulfate content. Heparin from various tissues varies in the proportions of these derivatives, and hence in its activity, unless they are separated by the isolation procedures, e.g., by preparation of the insoluble brucine derivative.

Astrup and Jensen have recently described their methods of preparation<sup>55</sup> and purification<sup>56</sup> of heparin. Their purest product resembles that of Charles and Scott and has a carbon content somewhat low for mucopolysulfuric ester. This difference would lose its significance were it to be shown that acetylation of the amino group was not constant in all units of the polymer. It is to be recalled that only about half of the theoretical quantity of acetic acid has been demonstrated by hydrolysis.

Strong support for the main contentions of Jorpes and his co-workers is to be found in the histologic investigations they have made of the distribution of heparin in tissues. Lison<sup>57, 58</sup> had shown that the metachromatic staining reaction given by mucoid and cartilaginous tissue with toluidine blue is due to the presence of mucitin- and chondroitinsulfuric acids, and that the reaction is specific for these sulfuric acid esters of high molecular weight. When the reaction was tested on heparin solution it was found that as little as 1.5 mg. in a liter of 0.01 per cent dye gave a distinct metachromatic shade, and 3 mg. gave a strong violet color, a precipitate gradually forming. The color with heparin is about one hundred times more intense than with chondroitinsulfuric acid.<sup>54</sup> The reaction given by heparin is precisely that given in tissues by the granules of the mast cells of Ehrlich, and in a very important paper Holmgren and Wilander<sup>21</sup> exhaustively discussed the morphology, chemistry, and function of these cells, and their relation to the heparin problem. Their distribution was investigated further, using the toluidine-blue reaction and a special fixing technique to escape the difficulties consequent to the water solubility of the granules. Mast cells were found to have a wide distribution in the several species studied, being particularly rich in the connective tissue surrounding blood vessels. The distribution was consonant with the existing data concerning the relative richness of various organs as sources of heparin. The ester sulfate content of tissues was found to parallel its content in mast cells, as was the content of crude heparin. The morphologic and chemical observations all strongly support the conclusion that (1) the metachromatic granules in these cells contain heparin, (2) that the cells have secretory activity, and (3) that their function is to supply the circulation with the physiologic anticoagulant.

heparin may be due to simultaneous combination with thromboplastic substance. This might explain the failure of protamine to shorten the coagulation time of normal chicken plasma,<sup>72</sup> i.e., to demonstrate the presence of small amounts of heparin in normal blood.

The quantitative relations between heparin and protamine and heparin have been examined,<sup>23</sup> 0.3 mg. of the former being neutralized by 1 mg. of the latter in vivo or in vitro. Protamine, however, is toxic when administered intravenously to dogs, although not to guinea pigs.

The toluidine blue reaction given by heparin has already been mentioned.

*(To be continued in the April issue. The additional references will accompany the second section.)*

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heparin is added to a neutral solution containing protein, the isoelectric point of the latter is shifted toward the acid side. Thus, in the case of globulin, the molecular combination with heparin is more stable on the alkaline side of the isoelectric point than before, and already precipitated globulin may be peptized by heparin addition. On the acid side of isoelectric point the protein is rendered less stable by heparin addition. This stabilizing effect of heparin in neutral solution is considered to be an important element in its anticoagulant action through prothrombin.<sup>60, 61</sup> The addition of heparin to albumin in weakly acid solution, and near its isoelectric point, produces flocculation, the insoluble complex being indistinguishable in several respects from globulin; in fact, this observation formed the basis of Fischer's theory that all the globulin fraction of serum arises from the action of antiprothrombin (heparin) on albumin.<sup>62</sup> That the heparin-albumin complex is actually globulin is generally denied, as it does not have the same solubility relationships in salt solutions as native globulin<sup>63, 64</sup> nor does its osmotic pressure,<sup>65</sup> molecular weight,<sup>66</sup> or immunologic behavior<sup>67</sup> differ from that of serum albumin, although it has lost the property of solubility at the isoelectric point.<sup>68</sup> The flocculating and peptizing action of heparin at certain hydrogen-ion concentrations has been confirmed, and forms the basis for Fischer's turbidity method of quantitative estimation of heparin. Fischer has shown that heparin and thromboplastic substance (cephalin) react stoichiometrically with the formation of a dissociable complex.<sup>32</sup> Schmitz and Kühl<sup>69</sup> found that the anticoagulant activity of heparin serum was quickly destroyed upon warming, and that even at room temperature inactivation rapidly occurred. Both the albumin and globulin fractions of serum were able to effect this when added to a buffer solution of the anticoagulant, presumably by the formation of some undefined complex. This is no doubt important in relation to the rapid return of the coagulation time to normal following intravenous injection of heparin.

Fischer and Schmitz<sup>70</sup> have also shown that heavy metals accelerate clotting in heparinized plasma, and attribute this to the formation of insoluble heavy metal salts of the anticoagulant. The silver ion is particularly effective in this respect. Various aspects of these properties of heparin have been summarized by Fischer and interpreted in terms of their relation to coagulation.<sup>71</sup>

The important observation that heparin and protamine combine chemically was made by Chargaff and Olson,<sup>24</sup> who found the anticoagulant effect of heparin to be abolished by protamine added *in vitro*, or administered intravenously. The nature of the heparin-protamine complex has been further studied by Chargaff,<sup>72</sup> who also found that protamine and cephalin likewise form an insoluble complex.<sup>73</sup> A part of the effect of protamine addition to blood containing

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skin in one sheet of absolutely uniform thickness from any area of the body in any pattern and of any thickness desired, practically eliminating the chance of either a failure of "take" or a partial failure of "take" and giving a good cosmetic appearance along with good protection. The device used by Dr. Padgett consisted of a large cylinder similar to a kymograph drum, which had a sharp knife with micrometer adjustment. The blade was made to move to-and-fro across the long axis of the face of the drum. At the start the skin was fixed to the drum with rubber cement and as it was sliced off the drum was rotated simultaneously, the skin adhering to it.

*Discussion.*—J. B. Brown, St. Louis, Mo., exhibited some slides illustrating various types of grafts and stages of healing. He discussed the confusion of the terminology of split grafts. H. W. Trusler, Indianapolis, Ind., presented slides showing the use of roll grafts, particularly emphasizing difficulties and failures with thick, split grafts in areas which still harbor infection and commenting on the importance of bacterial tests. Dr. Padgett referred to the economic advantages of his method in saving the patient time and expense.

IV. *Hypospadias, a Report on the Use of a Depilated Scrotal Flap*, Harry P. Ritchie, St. Paul, Minn.—Dr. Ritchie thought that the reason for the multiplicity of operations for hypospadias was the fact that the problem has been approached on a regional basis. The nature of the problem, he believed, was not dissimilar from many other situations in the body where loss of tissue required reconstruction by mobilization either of adjacent tissues or their transplant from more distant areas. He then described the advantages and disadvantages of a number of the operative procedures which have been used and urged as superior the operation utilizing flaps cut from the genitals. An illustrated case report showing the use of a tubed scrotal flap was presented.

*Discussion.*—Gatewood, Chicago, Ill., believes Ritchie's operation is sound but has seen many failures with various operations. He does not believe the growth of hair within these channels is as serious a complication as many have believed. J. B. Brown, St. Louis, Mo., feels that a method which makes more skin available is an advantage. He emphasized the importance of the first stage and the avoidance of injury to the corpora cavernosa. E. C. Padgett advocated the use of the Foley catheter as an aid in keeping the child dry. Dr. Ritchie agreed with Dr. Brown on the importance of proper release of the penile adhesions and described further the difficulties encountered in the case in question.

V. *Hemorrhagic Tendency in Jaundice, With Special Reference to Its Treatment With Vitamin K*, Waltman Walters and Albert M. Snell (by invitation), Rochester, Minn.—Dr. Snell outlined the present concept of the causes of bleeding in jaundiced patients or in persons with biliary fistula. This complication, he argued, was due to a deficiency of prothrombin, which in turn was the result of a lack of vitamin K. Failure of vitamin K absorption, he said, could be explained on the basis of the exclusion of bile from the intestine and the associated damage to the liver. He presented a series of operative cases showing the decrease in prothrombin and the effect of the administration of vitamin K and bile salts in establishing and maintaining a normal level of prothrombin preoperatively and postoperatively. He mentioned briefly the method of obtaining vitamin K either from extracts of rotted fish meal or alfalfa.

*Discussion.*—R. W. McNealy, Chicago, Ill., cited some work on 800 cases of jaundice observed at Northwestern University showing that postoperative bleeding could be controlled with bile salts and viosterol. He also discussed the importance of a lack of vitamin P. He suggested blood transfusion and intravenous glucose before operation if the bleeding time (Ivy) was prolonged. Dr. Snell found no



# Review of Recent Meetings

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## REPORT OF WESTERN SURGICAL ASSOCIATION, FORTY-EIGHTH ANNUAL MEETING, DEC. 2 AND 3, 1938, OMAHA, NEB.

J. M. McCaughan, M.D., St. Louis, Mo.

(From the Department of Surgery, St. Louis University School of Medicine)

I. Cystography in the Study of Difficulties Following Prostatic Surgery, Theodore H. Sweetser, Minneapolis, Minn.—Dr. Sweetser showed some excellent cystograms obtained by means of injecting air through a urethral catheter into the bladder. He emphasized that cystography was a valuable guide in the treatment of prostatic obstruction; also that it was of value in diagnosis in patients with various complaints after prostatectomy. He further advocated its use as a follow-up after secondary treatment of postprostatectomy sequelae.

*Discussion.*—Verne Hunt, Los Angeles, Calif., stressed the value of pre- and postoperative cystograms. He regards air as safe and simple but is loath to rely on it, preferring the opaque media as having more universal application. At any rate, he said the cystogram should be considered only one part of the examination. W. J. Carson, Milwaukee, Wis., prefers intravenous retention cystograms. Particularly, he likes to avoid the catheter in the presence of pyuria. The question of air embolism was raised by Dr. Carson. T. H. Sweetser, in closing, said he felt there was little danger of air embolism. In his experience radio-opaque solutions have not been as accurate as air.

II. An Improved Incision for the Radical Operation for Carcinoma of the Breast, Neil J. Maclean, Winnipeg, Canada.—Dr. Maclean discussed a new incision for radical operation for carcinoma of the breast. After discussing the importance of wide skin removal, he enumerated the difficulties of subsequent closure and showed illustrations of his technique which was essentially a T-incision with the vertical limb of the T directed laterally toward the axilla. The closure of the flaps, he said, now can be made without unsafe tension as is often the case with either the Halstead or other types of vertical incisions.

*Discussion.*—T. Orr, Kansas City, Kan., objects to any incision which places the scar across the axilla and said there was no one incision satisfactory for all breast cancers. A. E. Benjamin, Minneapolis, Minn., chooses the incision best suited to case. He questioned the resulting axillary scar in Dr. Maclean's incision. J. F. Perey, Los Angeles, Calif., believes Dr. Maclean's incision suitable for early cases but personally prefers to leave the wound open. He stated that "cosmetics had no place in the treatment of cancer." Dr. Maclean, in closing, stated he prefers the vertical incision in cases with involvement of the axilla. He has not seen as many instances of skin metastasis with this incision as with the vertical types.

III. The Calibrated Skin Graft. A New Principle and a New Type of Graft, Earl C. Padgett, Kansas City, Mo.—Dr. Padgett described a method of cutting

the Chicago area. He then discussed the pathogenesis, pathology, differential diagnosis, and treatment. W. Cole, St. Paul, Minn., emphasized the rarity of the lesion and the danger of confusion with osteomyelitis. Dr. Meyerding exhibited slides of additional cases.

**IX. Nonparasitic Cysts of the Liver: A Report of Two Cases and an Analysis of the Literature,** John M. McCaughan, and Louis J. Rassieur, St. Louis, Mo.—Dr. McCaughan reported two cases of nonparasitic liver cyst. The several theories which attempt to account for the origin of these cysts were mentioned briefly. A review of the literature and an analysis of a large number of the reported cases was made. This latter was done to see if a correlation of symptoms, physical and pathologic findings would yield data of diagnostic value. Treatment and its relation to the end results were discussed.

*Discussion.*—Dr. Rassieur discussed the difficulties of differential diagnosis and the need to have the condition in mind. He also outlined the method of treatment. F. F. Attix, Lewistown, Mont., cited an unpublished case of his own and exhibited some excellent illustrations showing the operative technique employed. R. Bartlett, St. Louis, Mo., reported also two unpublished cases and felt that in one instance had the cholecystogram not been misinterpreted a correct diagnosis might have been made. Dr. McCaughan cited the recent experimental work of Bogetto in Italy on the experimental production of single and multiple cysts of the liver in rabbits by the transplantation of gall-bladder epithelium to the liver.

**X. Single Trauma as an Etiological Factor in Carcinoma,** William E. Leighton, St. Louis, Mo.—Dr. Leighton presented an abstract of cancer histories from the Barnard Free Skin and Cancer Hospital with antecedent single trauma. No case was complicated by medicolegal or compensation considerations. He dealt with the evidence for and against single trauma as an etiologic factor in carcinoma.

*Discussion.*—H. Davis, Omaha, Neb., said that absolute proof was very difficult to obtain. He cited that a comparative study of war records did not indicate a higher evidence of cancer than that common to the general population in the same age group. Dr. Leighton exhibited photographs of two patients who developed epitheliomas on the face after razor cuts while shaving.

**XI. Indications for Splenectomy in Children,** George B. Packard, Denver, Colo.—Dr. Packard reviewed case reports of twenty splenectomies in young children. His series included patients with familial hemolytic uterus, idiopathic purpura hemorrhagica, splenic anemia, and splenomegaly with gastric bleeding. He also commented on other anemias possibly related to splenic disease and on Gaucher's disease. Following this he considered the criteria of positive indications for splenectomy and the preoperative and operative treatment.

*Discussion.*—A. Montgomery, Chicago, Ill., remarked that Dr. Packard's paper was timely because splenectomy has been performed somewhat indiscriminately. Mention should be made of splenectomy for trauma and for tumors of the spleen. George Curtis, Columbus, Ohio, said he had made special blood studies and examination of the splenic pulp and bone marrow in fifty-two splenectomies in an attempt to correlate these factors with the clinical course but the results were not striking. C. Johnston, Detroit, Mich., referred to several cases of icterus neonatorum gravis in which the blood changes were investigated after operation. E. Miller, Chicago, Ill., made a suggestion for improving the operative technique. Essentially his procedure is to retract the stomach out of the way and secure the entire splenic pedicle with a tourniquet before beginning the ligation of the individual vessels.

antihemorrhagic factor for chicks in pure fish oils. He had no experience with the Ivy bleeding time but did not think there had been any conclusive demonstration of the effect of vitamin P deficiency. He agreed with Dr. McNealy on the importance of proper preoperative preparation. F. W. Bancroft, New York, N. Y., recalled the work of Quick on prothrombin in 1925 when it was suggested that bleeding might be due to a protein deficiency. He also advocated the use of vitamin K.

**VI. Anesthesia, Anesthetic Agents, and Surgery, Erwin R. Schmidt, Madison, Wis.**—Dr. Schmidt said that the science of anesthesia, together with the art, has advanced tremendously in the last fifteen years, based on research and better knowledge of basic science, so that it is a distinct field in medicine. The best anesthesia which may be obtained in the various hospitals will depend, he believes, upon the different factors involved; namely, equipment, training of the anesthetist, and training of the surgeon. The latest developments in anesthesia were briefly described. The application of this newer knowledge, together with the introduction of an anesthetist into the surgeon's team and the role that the surgeon has to play for the fullest working-out of this new cooperative endeavor, was described.

*Discussion.*—W. H. Cole, St. Paul, Minn., considered Dr. Schmidt's emphasis of closer cooperation between surgeon and anesthetist as highly important. He discussed the value of oxygen therapy, the blood pressure level during anesthesia, and the proper choice of preanesthetic drugs. Gatewood, Chicago, Ill., discussed the importance to the surgeon of an understanding of the four planes of anesthesia and urged that surgeons aid in the development of facilities for training anesthetists. T. H. Sweetser, Minneapolis, Minn., questioned the use of ether anesthesia in elderly individuals. J. F. Percy opposed the indiscriminate use of barbiturates preoperatively and cited a fatal case in which the patient had been given ten or twelve different agents. He preferred ether in his own practice. Dr. Schmidt emphasized the need for judgment in the selection of the anesthetic agent to fit the particular patient's need. He recommended Gudel's monograph for the fundamentals of anesthesia.

**VII. Tumors of the Neck, William Boyd (guest speaker), Toronto, Canada.**—Dr. Boyd, introduced by N. J. Maclean, Toronto, Canada, discussed the diagnosis of tumors of the neck. He stressed the importance of approaching the diagnostic problem with orderly thinking. In respect to various classifications of tumors of the neck he mentioned two human traits common to most classifiers; namely, those who "split" and those who "lump." He then presented a systematic classification of tumors of the neck and described the pathogenesis, pathology, and differential diagnostic features of each. His presentation was augmented by many excellent photographs. Particularly good were several taken from Dr. Hertzler's monograph.

**VIII. The Diagnosis and Treatment of Ewing's Tumor, Henry W. Meyerding, Rochester, Minn.**—Dr. Meyerding reviewed the cases of Ewing's tumor encountered at the Mayo Clinic for a period of more than twenty-five years. He explained that this lesion was frequently confused with osteomyelitis by surgeon, roentgenologist, and even by the pathologist. The response to roentgen radiation was a diagnostic test of great value. Dr. Meyerding then dealt with the choice and results of treatment by irradiation, surgery, and a combination of the two.

*Discussion.*—R. D. Schrock, Omaha, Neb., presented a case in which both osteomyelitis and Ewing's tumor developed in the same extremity. K. Speed, Chicago, Ill., exhibited slides showing the distribution of Ewing's tumor, osteogenic sarcoma, and benign giant cell tumor. He said that Ewing's tumor was rare in

the Chicago area. He then discussed the pathogenesis, pathology, differential diagnosis, and treatment. W. Cole, St. Paul, Minn., emphasized the rarity of the lesion and the danger of confusion with osteomyelitis. Dr. Meyerding exhibited slides of additional cases.

**IX. Nonparasitic Cysts of the Liver: A Report of Two Cases and an Analysis of the Literature, John M. McCaughan, and Louis J. Rassieur, St. Louis, Mo.**—Dr. McCaughan reported two cases of nonparasitic liver cyst. The several theories which attempt to account for the origin of these cysts were mentioned briefly. A review of the literature and an analysis of a large number of the reported cases was made. This latter was done to see if a correlation of symptoms, physical and pathologic findings would yield data of diagnostic value. Treatment and its relation to the end results were discussed.

*Discussion.*—Dr. Rassieur discussed the difficulties of differential diagnosis and the need to have the condition in mind. He also outlined the method of treatment. F. F. Attix, Lewistown, Mont., cited an unpublished case of his own and exhibited some excellent illustrations showing the operative technique employed. R. Bartlett, St. Louis, Mo., reported also two unpublished cases and felt that in one instance had the cholecystogram not been misinterpreted a correct diagnosis might have been made. Dr. McCaughan cited the recent experimental work of Bogetto in Italy on the experimental production of single and multiple cysts of the liver in rabbits by the transplantation of gall-bladder epithelium to the liver.

**X. Single Trauma as an Etiological Factor in Carcinoma, William E. Leighton, St. Louis, Mo.**—Dr. Leighton presented an abstract of cancer histories from the Barnard Free Skin and Cancer Hospital with antecedent single trauma. No case was complicated by medicolegal or compensation considerations. He dealt with the evidence for and against single trauma as an etiologic factor in carcinoma.

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**XII. Technical Notes on Pediatric Surgery:** (1) Hypertrophic Pyloric Stenosis and (2) Congenital Indirect Inguinal Hernia, Stanley J. Seeger, Milwaukee, Wis.—Dr. Seeger stated that he considered the Ramstedt operation the standard treatment for hypertrophic pyloric stenosis. He discussed the prevention of wound disruption and stressed the importance of the high incision. The necessity for a proper appreciation of the anatomic arrangement in the pyloric area he regarded as essential if one were to avoid failure to relieve the obstruction. Puncture of the duodenum at operation, he said, was not serious unless it went unrecognized and unrepaired. He then showed illustrations of the proper technique. Dr. Seeger spoke of the technical steps in dealing with the *proecessus vaginalis* in congenital inguinal hernia and stressed basic anatomic considerations.

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**XIII. The Influence of Sutures on Operative Wounds,** Clifford U. Collins, and J. E. Bellas (by invitation), Peoria, Ill.—Dr. Bellas reported results of his researches on a new nonsuture material of nonanimal origin which he called plastigut. He demonstrated by means of photomicrographs the differences in tissue reaction with catgut silk and plastigut and explained that the first two, being foreign bodies of protein origin, always reacted more or less intensely, which in turn tended to hinder primary repair. He defined the characteristic of the hypothetical ideal suture and concluded from his experimental and clinical studies that in plastigut this ideal had been most nearly attained.

*Discussion.*—Dr. Collins compared the results with catgut, wire, and plastigut and found the last superior. The incidence of healing by first intention was increased and the patients could be out of bed at an earlier date. E. Schmidt, Madison, Wis., enumerated the criteria for the ideal suture material. He had used plastigut in experimental animals and humans with good results. W. J. Thompson, St. Louis, Mo., agreed in condemning the use of catgut and silk. He reviewed some personal experimental and clinical work with a new type of suture material obtained from animal membrane and exhibited slides to show satisfactory results. Dr. Bellas said that plastigut was a nonanimal substance derived from plastic

material similar to Dupont's lusite. In commenting on Dr. Thompson's work he questioned whether an absorbable material in the very nature of things could ever be entirely without reaction. He suggested that it might be very much delayed with Dr. Thompson's material. H. K. Bonn, Los Angeles, Calif., exhibited specimens of tubulized chromic catgut which he thought ideal for suturing a divided ureter or common duct.

**XIV. A Simple, Efficient Method to Diminish the Incidence of Primary and Secondary Infection in Surgical Wounds, Reginald H. Jackson and Reginald H. Jackson, Jr. (by invitation), Madison, Wis.**—Dr. Jackson, Sr., reviewed the methods of Hart and others to diminish air-borne infections in surgical wounds by sterilizing the air and considered other factors involved in primary wound healing. He proposed a simple method which in his experience has given satisfactory results. The method of Jackson was based on observation of frequent primary healing after soap and water cleansing of accidental wounds known to be contaminated. He used a soap made of soy bean oil and corn oil, saponified with potassium salts. Had 200 consecutive cases without a single infection. He then exhibited moving pictures in color showing the technique.

*Discussion*—Dr. Jackson, Jr., described the technique used by them in taking their moving pictures. O. H. Wangensteen, Minneapolis, Minn., recalled Listerian times and then questioned the advisability of permitting large numbers of visitors to witness operations. He also discussed the problem of masks and adequate bacteriologic control of the operating room and its equipment. H. W. Trusler, Indianapolis, Ind., has utilized the same principle of cleansing tissue advocated by Dr. Jackson. He cited a case of a skin graft which failed, he thought, because of *Streptococcus hemolyticus* organisms probably hidden in the scar. M. L. Mason, Rochester, Minn., cited the rate of growth of various organisms in tissues as a reason for early mechanical cleansing with soap and water. Dr. Jackson, Sr., emphasized again that there was no particular bactericidal virtue in the soap itself, but that careful mechanical cleansing was essential for best results.

**XV. Experiences With Employment of Suction in the Treatment of Acute Intestinal Obstruction: A Reiteration of the Indications, Contraindications, and Limitations of the Method, Owen H. Wangensteen, Minneapolis, Minn.**—Dr. Wangensteen reviewed his experiences since 1931 in the treatment of acute intestinal obstruction by means of suction applied to an indwelling duodenal tube. This included consideration of the indications, contraindications, and the limitations of the method and the importance of correlating well all clinical and roentgen data. He emphasized most particularly the importance of accurate differential diagnosis. An effort, he said, should be made to answer the following questions before blindly instituting treatment: (1) Is there intestinal obstruction? (2) Is strangulation present? (3) Is the obstruction in the small or large intestine? (4) Is the obstruction complete or incomplete? He then presented statistics showing the comparative results in 156 cases of acute mechanical obstruction. There were 57 cases in which suction alone was employed. The mortality in the entire group was approximately 18 per cent. The mortality in the cases decompressed satisfactorily by suction was 7 per cent.

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temporary improvement. He did not believe alleged local irritation of the tube of more than minor importance. A. Montgomery, Chicago, Ill., questioned erosion of the esophageal and gastric mucosa from irritation of the tube. Charles Johnston, Detroit, Mich., commended Dr. Wangensteen's contribution and emphasized the importance of introducing the tube past the pyloric ring, which in his hands was not always easy to accomplish. He cited eighty-seven cases of his own treated in this manner. Dr. Wangensteen described in detail his technique of introducing the tube and securing duodenal intubation. He answered Dr. Montgomery by citing a case which came to post mortem after fifty-six days of drainage. No erosions of the gastrointestinal mucosa were noted.

XVI. Peptic Ulcer, Intractable or Recurrent, F. Gregory Connell, Oshkosh, Wis.—Dr. Connell's paper dealt with the surgical management of intractable or recurrent peptic ulcers. He considered the etiologic and pathogenic factors and the complications to which these ulcers are subject. The pathologic physiology of hyperacidity was discussed and the necessity of diminishing the acid secretion rather than attempting solely to increase the neutralization factors was emphasized. Therefore, he advocated a combination of nonoperative (diet and antisecretagogues) and operative (vagus resection and partial fundusectomy) measures.

Discussion.—C. S. Williamson, Green Bay, Wis., commented on the failures of operative and medical treatment. He said that hyperacidity per se was probably not important unless the normal mechanism for neutralization was deficient and in support of this view cited the experimental work of Mann and Williamson on duodenal drainage. J. Berman, Indianapolis, Ind., discussed the relations of high gastric acid to ulcer and cited experimental work of the stimulation to mucin formation by Brunner's glands and the fact that low mucin values were found in patients with high stomach acids. He described a type of pyloroplasty which he favored. R. R. Best, Omaha, Neb., cited a recent case of intractable recurrent gastrojejunal ulcer in which he undertook an extensive resection.

XVII. The Management of Megacolon, Claud F. Dixon and J. A. Barger (by invitation), Rochester, Minn.—Dr. Dixon said that while sympathectomy might be of value in the treatment of Hirschsprung's disease in children and in patients under 20 years of age, in older individuals resection of the colon was the procedure of choice. In four of his cases treatment consisted in a removal of the entire colon with the exception of the lower sigmoid and rectum, after which the ileum was anastomosed to the rectosigmoid. The operative technique was demonstrated in a colored moving picture. The results from this type of management, he declared, had been most encouraging.

Discussion.—W. T. Peyton, Minneapolis, Minn., defended sympathectomy for megacolon and stated that while there might not be anatomic return to normal yet function may be improved. The general mortality of exteriorization, he felt, was too high. He advocated further study of ganglion cells in these cases. Dr. Dixon agreed that good function may follow sympathectomy in selected cases but regarded appendicostomy as inferior to either sympathectomy or resection.

XVIII. The Surgical Significance of the Motor Activity of the Human Stomach, George M. Curtis and Frank E. Hamilton (by invitation), Columbus, Ohio.—Dr. Hamilton reported studies on the motor activity of the human stomach, first under normal conditions and then the effects of unilateral and bilateral splanchnic resection, vagotomy, herniorrhaphy, and cholecystectomy. He reported that biliary diseases increased the activity of the stomach, while immediately following a laparotomy gastric motility was decreased up to three days; subsequently, a

hypermotility ensued. This increased activity was associated with the occurrence of "gas pains." The effects of morphine, atropine, ephedrine, and prostigmin upon the disturbed postoperative motility were investigated.

*Discussion.*—T. Orr, Kansas City, Kan., discussed the clinical applications of Dr. Hamilton's researches and cited his personal interest in the action of morphine and prostigmin on the stomach and intestines. Gatewood mentioned similar experiments in which he engaged several years ago. The results were somewhat different. He thought that the same patient might give variable results at different times. Dr. Hamilton answered Dr. Gatewood on the variability of results in the same patient by citing a case of vagotomy which gave identical results after an interval of two years.

XIX. Glimpses Into the History of Surgery (Presidential Address), Casper F. Hegner, Denver, Colo.

XX. The Treatment of Penetrating Wounds of the Lung, John M. Foster, Jr., Denver, Colo.—Dr. Foster called attention to the fact that the real mortality following lung penetrations occurred within a few minutes to a few hours following the accident as a result solely from a sudden, massive hemothorax and that any expectant means of treatment was obviously doomed to failure. The treatment of choice in his experience was early aspiration of the pleural blood with replacement by air. The advantages and technique of the collapse therapy were discussed in detail and illustrated with case reports.

*Discussion.*—W. D. Gatch, Indianapolis, Ind., emphasized the value of auto-transfusion and in desperate cases made the suggestion that the aspirated blood be citrated and part set aside for later use. G. E. Cheley thinks mortality still is too high, urges earlier diagnosis of exact nature of injury. He preferred surgery in the severer forms with large vessel injury at the hilus of the lung. J. D. Bisgard, Omaha, Neb., asked about air embolism. O. H. Wangensteen, Minneapolis, Minn., suggested that the coexistence of an unsuspected bronchial fistula might be the cause of the "irreducible minimum" in mortality figures. He urged early recognition of this complication. R. T. Vaughn, Chicago, Ill., likewise asked about the danger of air embolism. C. F. Hegner, Denver, Colo., described in detail the technique of the procedure. He felt that the compression would close a bronchial fistula. He stressed the point that the simplicity of the technique and apparatus needed made the method available anywhere and to anyone; whereas, the radical operation called for a high degree of experience and skill. Dr. Foster thought the idea of citrating part of the aspirated blood a good one. He said he had never seen air embolus follow the injection. He also described the technique of injection in detail.

XXI. Compound Fractures Around the Elbow Joint, Illustrated With Lantern Slides, William R. Cubbins, Chicago, Ill.—This paper discussed the treatment of compound wounds from an operative standpoint, from a prophylactic standpoint, with tetanus and gas antitoxin, and submitted a new method for extension, which essentially was the insertion of an ordinary screw type of hook into the ulna. He also described in detail the technique of suturing the olecranon to the triceps muscle. In dealing with compound fractures he urged thorough mechanical cleansing and complete débridement of the wound which was then to be closed loosely. Dressings, he said, should be of dry sterile gauze and should be changed every six hours to promote capillary drainage. Accurate immediate approximation of the bone fragments he considered secondary in importance to thorough cleansing of the wound. He preferred to give gas bacillus and tetanus antitoxin in massive doses rather than in the customary prophylactic amounts. He then outlined his method of treatment for active gas bacillus infections.

*Discussion.*—F. D. Dickson, Kansas City, Mo., stressed the importance of early recognition and immediate treatment. His experience with ordinary prophylactic doses of serum in these cases of potential gas bacillus infection has been satisfactory. J. Jackson, Madison, Wis., discussed injury to the brachial artery in anterior and posterior elbow joint dislocations and cited a personal case in which he successfully anastomosed a severed brachial artery. E. L. Gilcreest, San Francisco, Calif., commented on the importance of elevation of the elbow joint and proper position of the forearm, and also on the value of beginning early motion in fingers and toes. L. F. Barney, Kansas City, Kan., asked about débridement after a twenty-four-hour lapse. Dr. Cubbins said it was his practice to remove all dead or dying tissue when found.

**XXII. Repair of Eversion of Vagina, With or Without Pelvic Viscera, Lester D. Powell, Des Moines, Ia.**—Dr. Powell described an operation which utilizes the rectus fascia for the support of the vaginal vault or pelvic structures. His operation essentially is to dissect out a triangular flap from the rectus fascia. This flap is bisected and next the two halves are carried into the pelvis where they are attached either to the uterus, the cervical stump, or the tissues of the vaginal vault, as the case might be.

*Discussion.*—O. J. Fay, Des Moines, Ia., said that he had seen and examined both of Dr. Powell's cases. He had also used the operation on one patient with satisfactory results. V. C. Hunt, Los Angeles, Calif., thought Dr. Powell's operation possessed certain advantages over other procedures, particularly where the cervical stump could not be brought up for fixation. Dr. Powell said he would rather not have it referred to as the Powell operation until it had proved its worth.

**XXIII. Giant Cell Tumor of the Humerus, Percy D. Peabody, Webster, S. D.**—Dr. Peabody reported a case which became malignant after having been diagnosed as nonmalignant by experienced pathologists who studied the biopsy specimens and even the complete amputated specimen. Disarticulation of the shoulder was done and this was followed by rapid recurrence in the operative scar and early lung metastasis.

*Discussion.*—Wallace Cole, St. Paul, Minn., quoted Dr. Geschichter on the relative benign character of giant cell tumors but suggested that a small area of malignancy must have been overlooked. He urged closer correlation of the clinical, radiographic, and pathologic data. M. Henderson, Rochester, Minn., recalled his own impression of this case and enumerated some of the difficulties experienced in its study. K. Speed, Chicago, Ill., reported a case of his own in which a giant cell tumor was removed locally and five years later recurred with evidence of inguinal node involvement. Amputation was done but sections were not yet available. He thought either an osteogenic sarcoma or a malignant degenerative process in the giant cell tumor likely.

REPORT OF THE ANNUAL MEETING OF THE RADIOLOGICAL  
SOCIETY OF NORTH AMERICA AT PITTSBURGH, PA.,  
NOV. 28—DEC. 2, 1938

LEO G. RIGLER, M.D., MINNEAPOLIS, MINN.

(From the University of Minnesota)

AT THE annual meeting of the Radiological Society of North America many important papers on roentgen diagnosis and radiation therapy were presented. Only those of particular surgical interest will be reviewed here.

The value of the upright position in Gall Bladder Examinations was recapitulated by Alice Ettinger, Boston, Mass. She reviewed the work of Åkerlund and Bernstein and brought out the importance of this maneuver in the detection of small stones. In this manner is demonstrated the layering of bile in the gall bladder and the method by which concentration occurs. Cholesterol stones will float in iodine-containing bile, but not in normal bile. George Levene, R. M. Lowman, and E. G. Wissing, Boston, Mass., discussed the Roentgen Diagnosis of Strawberry Gall Bladder, pointing out that many cases of cholesterosis are diagnosed as normal by ordinary cholecystographic methods. They laid down certain criteria for the roentgen differentiation of the strawberry gall bladder from chronic cholecystitis, but failed to indicate convincingly how these findings differed from the normal.

The Roentgen Diagnosis of Union in Fractures of the Femoral Neck was discussed by L. H. Garland, San Francisco, Calif., who emphasized the difficulty of determining bony union in such cases. He believes that union cannot be predicted with certainty in less than twelve months after the injury, that weight-bearing must first be undertaken, and that bone trabeculae must be observed to extend across the fracture line before union can be established. Garland warned against appearances in the roentgenogram which simulate bony union.

A symposium on Low Back and Sciatic Pain was presented by a number of essayists. M. N. Walsh, of the Mayo Clinic, detailed the clinical and neurosurgical aspects of herniation of the intervertebral disk, emphasizing the frequency of this condition as a cause of low back pain. He presented data on 300 cases in which 332 herniations of the disk had been diagnosed. The use of clinical criteria, such as intractable low back pain or sciatica, the reversed Quackenstedt test, and the character of the spinal fluid, to select patients for myelography was detailed. P. B. Steele, Pittsburgh, Pa., emphasized the frequency of low back pain in the presence of normal roentgenograms, while R. S. Bromer, Philadelphia, Pa., demonstrated the numerous congenital anomalies and anatomic variations which might be observed roentgenologically, but whose clinical significance was not established. W. E. Chamberlain and B. R. Young, Philadelphia, Pa., reported on 150 cases of myelography, using  $O_2$  as a contrast medium. They find it satisfactory in many cases both for the diagnosis of intervertebral disk herniation and for cord tumors. It has the advantage that it is free from deleterious effects or dangers and when serious doubt occurs the examination may be repeated using lipiodol. They emphasized the importance of posture in the demonstration of ruptured disks, both during roentgen examination and at operation. J. D. Camp, of the

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Mayo Clinic, reported roentgen examination by myelography in 253 cases of spinal cord lesions, including 205 cases of ruptured intervertebral disk, 5 cases of thickened ligamentum flavum, and 43 cases of spinal cord tumor. The accuracy of diagnosis using 5 c.c. of lipiodol is extremely high both as to localization and as to the nature of the lesion. He believes there is no real harm done by myelography with iodized oil and is doubtful whether myelography with  $O_2$  is sufficiently accurate to justify its use. In the discussion Garland reported on 35 cases examined from one to twelve years after myelography with 5 c.c. of lipiodol, in none of which could be found any subjective or objective signs of cord or nerve injury due to the contrast substance.

E. J. Ryan, New York, N. Y., reported several cases of duodenal ulcer with the clinical syndrome of gall-bladder disease. He believes duodenal ulcer and cholecystitis are frequently associated, the gall-bladder disease being caused by the inflammatory process in the duodenum. The Roentgenological Differential Diagnosis Between Diverticulitis and Cancer of the Colon was presented by R. Schatzki, Boston, Mass. He pointed out that this differentiation must be made preoperatively largely on the roentgen findings as these conditions can seldom be distinguished at operation. The high mortality of resection in cases of diverticulitis makes it vital to determine which condition is present. He detailed the differential roentgen signs, emphasizing the importance of detailed examination of the local area with compression and "spot film" technique. The use of air is somewhat dangerous. In cases of obstruction in which the area of the lesion could not be filled with barium, he advocates preliminary cecostomy for relief of obstruction followed by re-examination roentgenologically within a week or two when the obstruction will usually have been relieved and visualization of the involved area can be obtained.

George White, Boston, Mass., described a method of impregnating soft rubber drains, such as the Penrose or cigarette drain, with barium sulfate, thus making it opaque to roentgen rays. It is possible to determine the presence and location of such a drain in an empyema cavity even if it is filled with fluid. The various properties of such a rubber drain are not impaired by such chemical preparation.

The papers on radiation therapy were presented largely in the form of symposiums. Carcinoma of the breast was discussed by a number of essayists. H. B. Hunt, N. F. Hicken, and T. T. Harris, Omaha, Neb., presented their work on roentgen diagnosis of breast diseases using contrast media. They advocate skiodan viscous (Winthrop) and  $CO_2$  insufflation. E. R. Whitmore, Washington, D. C., detailed his observations on the dissemination and metastasis of carcinoma of the breast by the use of whole organ sections. These demonstrate vividly the extensive infiltration of the breast tissue with cancer cells, in inflammatory carcinoma, the permeation of the lymphatics of the breast and fascial plexus, and extension to the liver. F. E. Adair, New York, N. Y., advised the use of aspiration biopsies of the breast in cases with palpable axillary glands followed by preoperative irradiation using very heavy doses of x-radiation. Six weeks later operation is done. This method is not used in the aged, in cases of lung fibrosis, or marked anemia.

C. F. Geschickter, Baltimore, Md., related his experiences with the use of subcutaneous pellets of estrin implanted in mice. By implanting in this manner long-continued, slow absorption occurred and with relatively small doses he produced mammary cancer. The statistical analysis indicates a definite correlation between the estrin and the development of the tumors. He also pointed out the necessity for examination of urine throughout the entire menstrual cycle if proper assays of prolactin are to be obtained.

A paper on Recovery Following Human Ovarian Irradiation was presented by H. W. Jacox, Pittsburgh, Pa., who reported a patient surviving five years after removal of a huge malignant ovarian tumor. In spite of extensive postoperative roentgen therapy followed by artificial menopause for three years, she later went through a normal pregnancy and puerperium and had a normal baby.

J. R. Carty and B. S. Ray, New York, N. Y., demonstrated a method of low voltage roentgen therapy of neurological tumors, directly applied with a mobile apparatus in the operating room, after exposure of the tumor. Some favorable effects have been observed. J. F. Kelly, Omaha, Neb., also presented the results of treatment with a mobile apparatus at the bedside particularly in cases of acute peritonitis, gas gangrene, surgical parotitis, pneumonia, acute osteomyelitis following compound fractures, post-partum infection, Ludwig's angina, erysipelas, and other infections. M. W. Berck and W. Harris, New York, N. Y., reviewed again their experiences with the roentgen treatment of bronchiectasis. In 80 cases, 50 per cent have had practically complete cessation of cough, foul expectoration, and toxemia. These patients achieve a social and economic rehabilitation and exhibit a "dry" bronchiectasis as the end-result.

A symposium on the differences between 200 kv. and supervoltage roentgen therapy brought out the conflicting opinions of a number of investigators. H. Schmitz, Chicago, Ill., reported on five-year end-results in carcinoma of the uterus and breast and believes his results are distinctly better using 800 kv. as compared to 300 kv. x-rays previously used. Likewise Richard Dresser, J. C. Rude, and B. J. Cosman, Boston, Mass., believe their results, especially in bladder tumors, were greatly improved by using 1,000 kv. x-rays. W. E. Costolow, Los Angeles, Calif., reviewed the five-year end-results using 500 kv. x-ray therapy especially in advanced cases of carcinoma of the cervix. He also believes the results are moderately improved over those obtained with lower voltages. In the discussion by various radiologists the numerous factors of error inherent in such comparisons were brought out. The opinion was general that no marked superiority of supervoltage radiation therapy had yet been clearly established.

## THE THIRD INTERNATIONAL GOITER CONFERENCE, WASHINGTON, D. C., SEPT. 12-14, 1938

F. T. H'DOUBLER, PH.D., M.D., SPRINGFIELD, MO.

THE Third International Goiter Conference was held in Washington, D. C., Sept. 12, 13, and 14, 1938. The two previous conferences were held in Berne, Switzerland, in 1927 and 1931. Undoubtedly the uncertain political situation in Europe, which was at a high pitch at the time of the Conference, was responsible for keeping away a number of participants. As it was, in addition to those from the United States, there were speakers from Switzerland, Cuba, Mexico, Argentina, Colombia, Poland, Roumania, France, Germany, and Italy, with Switzerland leading the foreign countries in the number of different speakers. All of the papers, except two, were read in English.

The American Association for the Study of Goiter caused its fifteenth annual meeting to occur at the same time and place as that of the Third International Goiter Conference and was host to the Conference. The meetings and programs of the two bodies were merged. There are no official connections between the Conference and the American Association as to membership; that is to say, membership in the one organization does not automatically require or furnish membership in the other.

Headquarters for the joint meeting were at the Mayflower Hotel, where on Monday morning, Sept. 12, the Conference was called to order by H. H. Kerr, Washington, D. C., chairman of the committee in charge of local arrangements. Very suitable greetings from the Honorable Cordell Hull, Secretary of State, were followed by a short address by Frank Lahey, Boston, Mass., President of the American Association for the Study of Goiter. Dr. Lahey gave his address in turn in English, German, French, and Italian.

The Conference proceeded to organization and election of officers. Frank Lahey was elected president and W. Blair Mosser, Kane, Pa. (secretary of the American Association for the Study of Goiter), was elected secretary. The following honorary presidents were elected: Theodore Lang, Munich, Germany; Henri Welti, Paris, France; H. Eggenberger, Herisau, Switzerland; S. Tubiazz, Warsaw, Poland; C. Wegelin, Berne, Switzerland; and Pedri Cossi, Buenos Aires, Argentina.

The organization then took up its scientific program. Fifty-five papers were listed for delivery over a three-day period. Obviously it would be very unsuitable in reporting this meeting to abstract each paper, and to abstract some and not others not only would amount to slights but also would impose upon the reader the reporter's bias of interest and importance. Consequently only the general trends of the meeting will be reported. Transactions of the meeting, including all the contributions read and those by title, can be had by communicating with Frederick A. Collier, Chairman, Ann Arbor, Mich.

The first portion of the beginning morning's program was given over to the subjects of endemic goiter, cretinism, and childhood myxedema. The direct relation of the incidence of endemic goiter and cretinism to the amount of geographical radioactive emanation and the inverse relation to geographical thorium emanation were brought out. A sharp distinction was made between childhood myxedema and

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cretinism. It was emphasized that geographical location is more important than any other factor (source of water, etc.) in relation to endemic goiter and cretinism. The second portion of the morning's program dealt with iodine metabolism (blood iodine levels, hormone iodine, urinary and fecal elimination of iodine) in relation to normal and abnormal thyroid function.

In the afternoon of the first day there was a variation of subjects ranging through studies of thyroid secretion, the effects of thyroid extract, thyroiditis, Riedel's struma, Hashimoto's struma, and malignant goiter. One of the high points of the meeting was the groups of papers on thyroiditis and malignancy of the thyroid and their discussions. The papers on malignant thyroid brought out that papillary tumors of the thyroid stand in one class regardless of origin and that with them prognosis is best, and that next in line in this respect is the malignant adenoma; whereas the prognosis is worse with the diffuse type with polymorph infiltration, and with the lymphosarcoma. The degree of malignancy of a thyroid tumor might be said to be proportional to its departure from the papillary form. Such factors as the patient's age and general condition, sensitivity of tumor to radiotherapy, histology pattern, etc., were discussed as was also the relation of time of discovery of malignancy (before, during, or after operation) to prognosis.

In the evening a very convincing group of papers was read on goiter prophylaxis, showing the efficacy of iodine both in Europe and in widely separated places in America.

The morning's program of the second day dealt with endocrinology in general (the combinations of disturbances of fourteen hormones can create 15,000,000 different changes!), the pituitary in relation to metabolism (describing a pituitary hormone that depresses carbohydrate metabolism, probably decreases protein metabolism, and greatly increases fat metabolism), the relation of pituitary to thyroid disease, the relation between vitamin A deficiency and thyroid disease, embryologic considerations relating to the thyroid, and sterol deposition after thyroidectomy. In the afternoon there was a wide variation of subjects including several on carbohydrate metabolism and several on the pituitary thyrotropic hormone. George W. Crile, Cleveland, Ohio, read a very fine paper on the Mechanism of Hyperthyroidism.

At the annual business meeting of the American Association for the Study of Goiter, J. K. McGregor, Hamilton, Ontario, was elected president; Claud Hunt, Kansas City, Mo., vice-president. W. B. Mosser, Kane, Pa., George C. Shivers, Colorado Springs, Colo., and V. E. Chesky, Halstead, Kan., were re-elected corresponding secretary, recording secretary, and treasurer, respectively.

The official banquet of the Conference was held in the evening.

On the final day in the morning session papers were given on experimental studies of exophthalmos and on the pathology of thyroid activity; also papers on various phases of thyroid disorders (anxiety overstimulation, toxic adenoma, hyperthyroidism with low basal metabolic rate, goiter heart, and recurrent hyperthyroidism) and a paper on iodine thyrotoxicosis. In the final afternoon the papers dealt with the medical treatment of hyperthyroidism, the use of vitamin B<sub>1</sub> in preoperative preparation, x-ray therapy, recurrent thyrotoxicosis, fallacy of iodine therapy after bilateral thyroidectomy, and hyperthyroidism in children; the discussion of the latter was accompanied by interesting x-ray films showing advanced skeletal development, the opposite of that found in cretinism or childhood myxedema. Frank Lahey, the president of the Conference and of the American Association for the Study of Goiter, read an excellent paper on Surgery in Hyperthyroidism, pointing out that in borderline cases firmness of the gland tends to point to toxicity. He advocated adequate exposure (furnished by cutting the muscles), a dry field, good light, and magnification, in identifying and thereby avoiding removal of or injury to



the parathyroids. Tissue removed should be inspected for parathyroids and any found should be transplanted. He also advocated demonstration of the recurrent laryngeal nerve to protect it against injury.

Allen Graham, Cleveland, Ohio, and his committee deserve much credit for their fine work in arranging so splendid a program.

## ANESTHETISTS' TRAVEL CLUB MEETING, OCT. 10-15, 1938

EDWARD B. TUOHY, M.D., M.S.(ANES.), ROCHESTER, MINN.

*(From the Section on Anesthesia, the Mayo Clinic)*

THE meeting of the Anesthetists' Travel Club was held at Madison, Wis., on Oct. 10 and 11; at Rochester, Minn., on Oct. 12 and 13; and at Minneapolis, Minn., on Oct. 14 and 15. The clinical demonstrations and seminars in anesthesia at Madison were conducted at the Wisconsin General Hospital by R. M. Waters and his associates. Inhalation anesthesia was demonstrated for a variety of surgical cases, using predominantly cyclopropane. The intratracheal method of general anesthesia with cyclopropane as the anesthetic agent was used frequently. The technique of controlled respiration for patients anesthetized with cyclopropane was demonstrated by various members of the department. The seminars in anesthesia and related subjects conducted at the Wisconsin General Hospital were given by various members of the university staff, including W. J. Meek, professor of physiology, who presented a paper on vasoconstrictors. He and his associates have been studying epinephrine, eobefrin, synephrin, neosynephrin, arterenol, paredrine, and many other sympathicomimetic drugs and it is their opinion that the toxicity of neosynephrin on the heart determined by electrocardiographic studies on dogs is the least of any of the vasoconstrictors studied.

An interesting discussion of the relationship of vitamins to anesthesia and of the transportation of oxygen and carbon dioxide in the blood was presented by several members of the Department of Agricultural Physiology. The importance of vitamin B in relation to the yellow respiratory enzyme of Warburg was discussed also.

In Rochester the Travel Club attended the clinical and experimental demonstration on anesthesia and related subjects held at the Mayo Clinic. The use of local and regional, intravenous, and inhalation anesthesia was demonstrated at the various hospitals by members of the Section on Anesthesia. The research work that is being carried on in anesthesia was demonstrated at the Institute of Experimental Medicine. T. H. Seldon demonstrated the activity of the capillaries in the ears of normal and anesthetized rabbits. L. H. Mousel presented a new device for the administration of inhalation anesthetic agents to small animals. E. J. Baldes, J. F. Herriek, and H. E. Essex demonstrated a new electrical method of measuring blood flow and blood pressure in animals.

A symposium on anesthesia was presented at the general meeting of the staff of the Mayo Clinic, which included a presentation by E. J. Delmonico on Tests for Derivatives of Barbituric Acid, one by L. H. Mousel on Effect of Some Respiratory Stimulants on Experimental Animals Anesthetized With Pentothal Sodium and one by J. S. Lundy on A Closed Method of Venipuncture and a Hand Roller for the Speedy Administration of Blood or Solutions for Intravenous Therapy. Another seminar and discussion in anesthesia and related subjects in-

cluded a presentation by C. J. Betlach on Effect of Various Anesthetics on the Electrocardiogram; by P. W. Searles on Effect of Certain Anesthetics on the Blood and by D. V. Shepard on Blood Transfusion. Discussions were given by E. J. Kepler on Diabetes as an Anesthetic Risk and by C. K. Maytum on Helium and Oxygen Treatment of Intractable Asthma. L. H. Mousel gave a presentation on Gas Analysis by the Effusion Method. W. M. Boothby and W. R. Lovelace demonstrated A New Type of Inhalation Apparatus for the Administration of Oxygen or Oxygen and Helium.

Members of the Anesthetists' Travel Club spent Oct. 14 and 15 as guests of Ralph Knight and his associates at the University of Minnesota. Members of the Department of Physiology under the direction of A. D. Hirshfelder and R. N. Bieter and their associates demonstrated the injection of pressor drugs in spinal anesthesia in rabbits. The results of their experiments indicated that pitressin combined with other pressor drugs, such as epinephrine, ephedrine, neosynephrin, and others, gave better results in the maintenance of blood pressure than did any of these other pressor drugs used alone. In the Department of Physiology, M. B. Visscher and his associates presented studies of dynamics of the heart during anesthesia by means of the Starling heart-lung preparation from a dog. The method of preparation of the heart-lung experiment was demonstrated to the group. Dr. Visscher is carrying on studies on the effect of many anesthetic drugs on cardiac output. Dr. Visscher showed that the output of the heart was diminished by about 30 per cent when sodium amytal was administered to the heart-lung preparation. The decrease in cardiac output was accompanied by a fall in mean blood pressure and a decrease in coronary circulation. R. T. Knight presented a clinical demonstration which included the technique of peridural anesthesia and various methods of regional and general anesthesia.

J. R. Paine of the Department of Surgery of the University of Minnesota gave a demonstration for measuring the elasticity of the human lung. This is computed on the basis of the amount of force producing distortion in the pleural cavity in relation to the amount of "distortion produced by that force." Pneumothorax is performed and by means of a water manometer variations in pressure are determined. The pneumothorax needle is connected by means of a rubber tube to a chamber in which there are two mirrors, a tidal air mirror and an intrapulmonary pressure mirror, and the patient breathes through an apparatus consisting of a large number of small brass tubes. The mirror is attached on a tambour and is deflected by the flow of air. The light from this mirror registers on a moving photographic film. The developed film shows a continuous line alternately above and below a base line and from this the elasticity of the lung is measured. The definite clinical value of such an estimation has not yet been established.

After attending the clinics on anesthesia and surgery at the University Hospital, members of the Travel Club were taken through the manufacturing plant of the Heidbrink Company and were shown various anesthesia apparatus.

# Book Reviews

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**The 1938 Year Book of General Surgery.** Edited by EVARTS A. GRAHAM, Washington University, St. Louis, Mo. Cloth. Pp. 781, with 312 illustrations. Chicago, 1938, The Year Book Publishers. \$3.

The idea of a year book in which the most important contributions to surgical literature are reviewed and the most significant advances discussed is a good one. A book of this sort, abstracting its articles almost solely from surgical literature, has of necessity a very definite practical objective in mind. Surgery, however, draws upon a wider range of knowledge than that concerned with diagnosis, recognition of the nature of pathologic conditions of surgical interest, and surgical technique. The reviewing of important articles in the interphase interests between surgery, bacteriology, biochemistry, and physiology would enhance the value of this work without detracting from its essential practical nature.

The Year Book Publishers are fortunate in having a man of the breadth and depth of view of Dr. Graham as its editor. That the editor knows his year book is apparent to anyone who thumbs through the pages of this volume. His acquaintance with the materials of previous year books is astounding, an observation which suggests that the editor enjoys the arduous tasks involved in the difficult labors of digesting literally thousands of articles. Very pertinent comments are made by him upon a large number of the abstracted reviews throughout the volume.

The entire range of surgery, except for the special provinces of the urologist, gynecologist and eye, ear and nose specialists, are reviewed. It would be difficult to mention, let alone select, the most significant contributions reviewed. The editor's introduction affords, in a way, a suggestion as to what he considers some of the more important material digested in the *1938 Year Book*. The writer of this review would commend especially the sections on anesthesia, asepsis, operative technique, and wound healing as containing much fundamental information for the enlightenment of all surgeons.

*The Year Book* is a handy reference manual to the surgical literature of the year and a valuable book for every surgeon to have within ready reach.

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**Meningiomas. Their Classification, Regional Behaviour, Life History, and Surgical End Results.** By HARVEY CUSHING, M.D., with the collaboration of LOUISE EISENHARDT, M.D. Pp. 785, with 685 illustrations. Springfield, Ill., and Baltimore, Md., 1938, Charles C. Thomas, Publisher. \$15.

Dr. Harvey Cushing, in collaboration with Dr. Louise Eisenhardt, presents a book on the meningiomas which is a fitting successor to the senior author's classic series of articles and monographs on tumors of the brain and spinal cord. The meningiomas are perhaps the most fascinating and difficult type of tumor which confronts the neurosurgeon. They make up only about 13 per cent of cerebral neoplasms, but are more frequently encountered than any single type of glioma. Nearly always a curable condition, provided they can be completely enucleated, they constitute a most stimulating challenge to the skill of the operator because of their all too common tendency to grow in inaccessible places, their vascularity, and the knowledge that they are liable to recur sooner or later unless their attachment to the dura and skull is thoroughly destroyed.

Three hundred and thirteen case histories with a follow-up period of from five to twenty-seven years form the background on which this book is built. Of these meningiomas, 18 originated in the spinal canal, the remainder within the skull. Only 2 of this long series of patients have been lost sight of. This gives an unparalleled opportunity to study the life history of this important group of tumors and to draw conclusions as to the most suitable method of surgical attack. It is also fascinating to trace the evolution of Dr. Cushing's technique. The operative mortality in the series of intracranial meningiomas operated upon in Baltimore prior to 1912 was 25 per cent. Through steady improvement this fell to a minimum of 8.3 per cent during his final five years at the Brigham Hospital. This dramatic change coincides with the increased use of blood transfusion, the reduction of excessive intracranial pressure by ventricular tap, saline irrigation of the wound and suction, also with such technical improvements as the silver clip and electrosurgical devices developed in Dr. Cushing's clinic.

Twenty-eight chapters of the book are devoted to a discussion of meningiomas in different areas. These are taken up in order of their geographical location, beginning with the rare instances without dural attachment and the infrequent tumors in the posterior fossa. This regional classification is continued up the base of the skull into the middle and anterior fossae, and then along the falx and out into the cranial convexity. Chapter 31 is devoted to the extraordinary case histories of two patients with recurring paracentral meningiomas on whom Dr. Cushing was forced to operate eleven and seventeen times respectively for rapid recurrences of the growth.

The four other chapters deal with historical aspects of the subject, a pathologic discussion of the meningiomas, a résumé of the intraspinal tumors, and an account of surgical technique and end results. It is of interest to note that one of the earliest cases in the series is alive and well 27 years after operation. Twelve other patients survived for over 20 years and an additional 67 for over 10 years. All together 132 patients are alive at the time of publication, 5 years after the last of the series was operated upon.

In conclusion the reviewer wishes to state that this work has given him greater pleasure than any other which it has been his privilege to review. It contains a wealth of material of great scientific value and references to over five hundred articles in the literature. The book is to be commended not only for the exceptional interest of its subject matter, but also for its readability and the uniform excellence of its 685 illustrations, which accompany nearly every page of the text.

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**Les Embolies Arterielles Des Membres.** By H. Haimovici. Paper. Pp. 333, Paris, 1937, Masson et Cie. 55 francs.

In this monograph the author presents an extensive review of the European literature dealing with the problem of embolism of peripheral arteries, but his major conclusions are largely those of his teachers, R. Leriche and J. Fiolle. The material is presented in the form of a thesis. The author stresses the value of the collateral vessels and he describes clearly the mechanism and conditions under which an active collateral circulation establishes itself. The surgical methods of embolectomy and arteriectomy are presented as the most important therapeutic measures, but no mention is made of the frequency of secondary intravascular clotting of the blood at the site of the surgical operation on the artery. The author likewise has failed to take into consideration the important contributions concerning the effect of heparin upon the intravascular clotting of blood. The general care of the affected extremity and other conservative methods of treatment are entirely omitted. On the whole, the material is presented rather dogmatically and the author

does not seem to realize that there is still much to be desired from all the present modes of treatment of these serious clinical problems. The monograph should prove valuable to those who are especially interested in peripheral vascular disturbances since it does contain a good summary of the important clinical, pathologic, and therapeutic aspects of major and minor arterial accidents.

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**The Vitamins and Their Clinical Applications.** By W. Stepp Kuhnau, Director of the Municipal Institute for Balneology and Metabolism, Wiesbaden, and H. Schroeder. Translated by Herman A. H. Bouman. Cloth. Pp. 173. Milwaukee, 1938, Wisconsin Cuneo Press, Inc.

This little manual on vitamins summarizes well the available information upon this important field up until 1936. In an appendix is included a larger list of English and American bibliographic references relating to the textual matter prior to and subsequent to the appearance of this monograph by its German authors. The appendix also contains brief sketches of the apparent function of each vitamin, the possible results of deficiency, as well as the results of absence of the vitamins in the diet.

In each chapter the historical aspects relating to the development of knowledge concerning the vitamin under consideration are briefly traced; the chemistry and occurrence of the vitamin, its mechanism of action, dosage, and man's requirement of it are discussed fully.

There is no field of medicine in which a knowledge of the vitamins is unimportant. Every practitioner would do well to acquaint himself with the advances which are being made in this aspect of nutrition. This monograph should prove a useful guide for the accomplishment of that purpose.

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**Industrial Surgery. Principles, Problems, and Practice.** By Willis W. Lasher. Pp. 452, with 193 illustrations. New York, 1938, Paul B. Hoeber, Inc. \$6.

It is difficult to recognize the need for a book such as Willis W. Lasher's *Industrial Surgery*. The surgery of trauma can be differentiated from the surgery of disease; but it is after all surgery, governed by the same fundamental principles of anatomy, physiology, and pathology. Industrial surgery, so-called, is surgery, largely traumatic, applied to groups of workmen. Except for entirely extrinsic factors, such as pre-employment examination and compensation, it is no different from surgery applied to any other group. There is perhaps a place for a text, written from the point of view of the experienced physician, on the medico-legal aspects of surgery under compensation conditions. Any attempt to present surgical disease seen in industrial practice—and this book represents such an attempt—must necessarily, to be of value, be exhaustive both from the fundamental and the practical points of view. It must, in fact, be a complete and authoritative monograph on the surgery of trauma.

Unfortunately the present volume fulfils this requirement neither in completeness nor in authority. Furthermore, its arrangement and presentation are confusing and often obscure. Although a section on surgical pathology occurs, there is no reference to the healing processes in wounds of the soft parts. The treatment of this commonest of industrial accidents is accorded six lines for the entire subject of débridement, hidden away under a subsection entitled "Antiseptics." Burns are discussed only under the heading of "Injuries of the Face,

Including Nose, Eyes, and Ears." Three pages are given without adequate reference to the profound systemic effects of these injuries. The toxin theory is accepted without reservation. There is no mention of shock or blood concentration and there are no recommendations for their treatment. Carron oil is accepted as the preferable medium for immediate application to the burned area.

These are examples only. The discussion of almost any subject chosen at random will be found to be incomplete, with evidence of confusion in fundamental ideas and with an intensely personal point of view. The phrases "in our opinion," "we believe," and the like occur on almost every page. Ludicrous mistakes are found; such as, "Creatine is a substance which makes up the ectoderm of arthropods and is almost identical with cartilage." The use of the same case material is in at least one instance exactly duplicated without reason (pages 47 and 322). The wrinkling of adhesive plaster strapping shown to illustrate the treatment of sprain of the ankle would not be permitted on the part of a second-year student. Finally, sentence structure is often so faulty as to obscure the meaning, and actual solecisms are frequent. One example may be cited: "Lacerations of the scalp should be drained [sic] with a small rubber band. They migrate rapidly, producing large pockets of pus. . . ."

Surgeons occasionally encountering industrial injuries may find useful the brief summaries of compensation equivalents in New York State, which appear at the ends of the chapters.

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**Essentials of Pathology.** By Lawrence W. Smith and Edwin S. Gault. Fabrikoid. Pp. 850, with 679 illustrations, New York, N. Y., 1938, D. Appleton-Century Company, Inc. \$9.

The authors have written a new type of textbook in which the case-history method of teaching is employed extensively. Most of the illustrations are accompanied by a full clinical history of the corresponding case. The large size of the book is due partly to the inclusion of 295 case reports. These have definite value in most instances, but they are often packed with irrelevant and tedious details. For example, fatty metamorphosis of the liver is illustrated not by a case of chronic alcoholism but by one of primary hypertension. A long story of a mixed tumor of the parotid gland illustrates mucoid degeneration. It would be advantageous to condense the case histories, especially in the sections dealing with general pathology. The teacher who uses this book, of course, must prepare separate case histories to correspond with his own teaching material.

The text is profusely illustrated. There are 679 figures on 160 large plates and 11 of the plates are in color. Most of the illustrations are good, but there are many poor photomicrographs. Because of the space required for case histories and illustrations, the text has been compressed unduly. The discussions are in many instances vague and evasive and betray a lack of wide reading and experience. For example there is a very sketchy discussion of edema on page 46 and on page 415 it is stated the incidence of coronary disease is many times greater in those subject to mental strain than in the phlegmatic.

There are good chapters on the avitaminoses, yaws, and animal parasites.

There are no references to the literature, the authors maintaining that very few medical students ever look up a reference. Medical students may not object to this innovation but the teachers of pathology probably will not take it kindly.

Notwithstanding the weaknesses which have been indicated this book is on the whole of much value. The generous illustrations make it particularly useful to the beginner and some teachers may like the case-history type of presentation.

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**Clinical Roentgenology of the Digestive Tract.** By Maurice Feldman. Cloth. Pp. 1014, with 357 illustrations. Baltimore, 1938, William Wood and Company. \$10.

This unusual monograph will fill a long felt need by clinicians. Within its pages the author recounts the clinical and roentgenologic aspects of all diseases of the digestive tract and its appendages. The number of rare diseases concerning which information is made available in this text is astounding. Intussusception of the jejunum into the stomach through the stoma after gastroenterostomy, hypertrophy of the pylorus of the adult, and other rare occurrences are given thoughtful consideration. It is somewhat surprising to note that the author omitted mention of the inverted position in detection of the site of occlusion in imperforation of the anal canal and rectum, a helpful roentgen finding.

The author's object in writing the book was "to bring together sources of material which have not heretofore been compiled in a single volume." Surgeons, internists, and roentgenologists owe a debt of gratitude to the author for this worthwhile accomplishment. It should prove an extremely valuable source book.

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**A Manual of Surgery for Nurses.** By Charles Wells. Pp. 490, with 160 illustrations. Baltimore, 1938. William Wood and Company. \$4.

This manual covers a very difficult field in a satisfactory manner. The author evidently realizes the inadequacy of the general preliminary training of the nurse and the difficulties thus encountered in her understanding of the problems of surgery. He takes nothing for granted and thus is able to describe the general field of surgery in a very simple and unostentatious manner. This method of attack does lend itself to some criticism, however, in that in many instances the subjects are dismissed with too little attention. In spite of this brevity, the vital points of the subject are covered and undoubtedly adequately enough so that they will remain fairly distinct entities in the nurse's mind, which might not be the case if the text were lengthy.

A favorable aspect of this work is that, although it is primarily intended to give a nurse some conception of surgical conditions, in each instance where nursing care is of paramount importance, the author has designated what the special duties of the nurse shall be.

Included in the text are 159 pen-line, black and white drawings, besides a frontispiece showing the thoracic and abdominal viscera.

The text includes the surgical specialties of urology, gynecology, and orthopedics, as well as eye, ear, nose, and throat.

The chapters are divided on a regional basis and include all of the more common, important diseases. The rare diseases fortunately are not mentioned.

The discussion of each disease is limited mainly to a description of the pathology of the disease and treatment. The diagnoses and differential diagnoses are not emphasized, as they are not in the province of the nurse and would only serve to confuse her.

This book is recommended for those nurses who are taking a preliminary course in surgery. It will give them an excellent understanding of the basic problems of surgery. For those doing postgraduate work and for those who are specializing in surgical nursing, it should be supplemented by other reading.

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**Digestive Tract Pain.** By Chester M. Jones. Cloth. Pp. 152, with 5 illustrations, New York, 1938, The Macmillan Company. \$2.50.

In this small monograph the author relates a summary of observations dating back over a period of fourteen years, during which time he has been investigating digestive tract pain. The technique involved concerned the swallowing of a small inflatable rubber balloon attached to a fine rubber tube by the subject under investigation. The position of the tube was checked by fluoroscopy. Overdistending a short segment of the alimentary tract induced spasm and caused pain. In his observations on pain in the pelvic colon and rectum, the author observed that twelve feet of tube on the average sufficed to permit the tube to reach from mouth to rectum.

The author investigated the production of pain in the esophagus, stomach, duodenum, ileum, and jejunum, as well as the various segments of the colon. Scatterograms are employed to indicate the location of the distress produced. Selected case histories occupy about one-half of the text. A concluding chapter on therapeutic considerations relates briefly the author's attitude toward the management of various types of abdominal ills. A few well-chosen references are appended.

This small text will be read with engaging concern by all interested in digestive tract pain, a fairly common denominator of diseases of the alimentary canal. Whereas the scatterograms indicate a certain constancy in the sites at which spasm of a segment of the digestive tract provokes pain (a feature particularly notable in the cecum), yet the clinician will find little encouragement that abdominal pain presented by a patient may now be interpreted with greater ease or more precision. However, he who reads this text with the care and attention that it merits will acquire a better understanding of the mechanism of digestive tract pain.

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**Surface and Radiological Anatomy.** By Arthur B. Appleton, William J. Hamilton, and Ivan C. C. Tchaperoff. 338 illustrations. Baltimore, 1935, William Wood & Company.

There is an increasing tendency in the modern teaching of anatomy to devote considerable time to practical application. That the study of normal, living anatomy can be best made through the medium of roentgenology is well understood. It is curious, therefore, that so little time is devoted to this phase of anatomy in many medical schools and that no text devoted exclusively to this study has heretofore been published. The volume under consideration combines a study of surface anatomy, clinical applications, and roentgen anatomy. At first thought there seems little connection between the first subject and the third, but the correlation of these two is due to the fact that both are a part of any system of clinical anatomy. The authors present in brief form the principal anatomical features of the body surface with adequate explanations of their significance and relationship to underlying structures. They correlate these with clinical methods of examination, such as percussion, bronchoscopy, and so forth. In addition they



describe briefly, but adequately, the normal roentgen appearance of the same anatomical parts, including the skeleton and those viscera which can be demonstrated by this method.

The subject of normal roentgen anatomy, if treated in reasonable detail, especially if normal variations are included, would be sufficient in itself to justify a good-sized text. The authors have been sufficiently concise and sufficiently gross in their general treatment so that the work is well balanced. The illustrations are numerous and well reproduced. The roentgenograms are clear, for the most part well labeled, and are often accompanied by correlating anatomical diagrams. A few anatomical variations are presented, such as the azygos lobe of the lung, although the far more common inferior accessory lobe is omitted. The development of the skeleton is presented by roentgenograms and a table of ossification centers is included in the appendix. The latter is sufficiently accurate for clinical purposes, but it should be noted that the epiphysis for the tuberosity of the fifth metatarsal is not given.

The correctness of the position of the left atrium on the roentgenograms of the heart is open to question. An elaboration of the description of the bronchial tree and of the significance of the linear markings of the lungs would be of value. In general, however, there is little to criticize other than the brevity of the work, which is, at the same time, a virtue.

This book may not be fully suitable as an applied anatomy for surgeons nor is it sufficiently detailed to completely serve as a normal roentgen anatomy for radiologists. For the student of anatomy, for the practicing physician, and for the beginning student of radiology, this volume will be instructive and of great practical value. It is a most valuable accessory to the usual text on gross anatomy.

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#### **Essentials of Obstetrical and Gynecological Pathology With Clinical Correlation.**

By Marion Douglas and Robert L. Faulkner. Pp. 187, with 148 illustrations. St. Louis, 1938, The C. V. Mosby Company. \$4.75.

This volume is primarily designed to be of value in teaching the essentials of gynecological and obstetrical pathology to medical students and resident staffs of hospitals, as well as to men who have been engaged in active practice and who have not had the opportunity to study even a minimal amount of pathology.

In 155 pages, in which are included 126 illustrations and smatterings of symptomatology and treatment, the authors endeavor to present the essentials of gynecological pathology. In the remainder of the volume, 21 pages, containing 42 illustrations, the essentials of obstetrical pathology are presented. Though arranged in excellent sequence and though the photomicrographs are excellent with very explanatory notes, the reviewer believes that this volume falls far short of presenting material that he would consider as essentials of gynecological and obstetrical pathology. The material, though well presented, is too sketchy and is not complete enough even to fall under the caption of essentials. There is no bibliography.

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## Original Communications

### TREATMENT OF THROMBOPHLEBITIS BY NOVOCAIN BLOCK OF SYMPATHETICS

#### TECHNIQUE OF INJECTION

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THROMBOPHLEBITIS occurring postoperatively, during or following many other conditions, is at best a very disabling disease and all too frequently terminates tragically. Numerous experimental and clinical investigations have been done in an attempt to elucidate the pathogenesis and development of this enigmatic phenomenon. In another publication,<sup>1</sup> the multifarious hypotheses and the numerous etiologic factors are reviewed and discussed in detail. The great variety of causes is indicative of the paucity of knowledge concerning the true mechanism. This is probably responsible for the wide differences in opinion regarding types of therapy, some of which are diametrically opposed. However, no attempt will be made here to discuss the sundry pathogenic factors and therapeutic measures as they have been adequately reviewed in another publication.<sup>1</sup>

Based upon our recent experimental and clinical investigations, we believe that heretofore the conceptions of the mechanisms producing the clinical manifestations in thrombophlebitis have been incorrect. In 1934, Leriche and Kunlin<sup>2, 3</sup> reported three cases of acute postoperative phlebitis which were successfully treated by novocain block of the lumbar sympathetic ganglia. Since this time Leriche and his co-workers<sup>4-6</sup> have reported other cases with similar results. According to Leriche,<sup>2, 3, 6</sup> the mechanism of the development of the clinical manifestations in thrombophlebitis is the initiation of a vasomotor reflex as a result of impulses originating in the thrombosed venous segment. Apparently Leriche is of the opinion that there are three dominant factors

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in this process; namely, venospasm, extent of coagulation, and arteriospasm.<sup>6</sup> Of these, venospasm is most constant and significant. By blocking the sympathetic ganglia with novocain, this vasomotor reflex is broken and the clinical manifestations relieved. This method has been successfully used by Bourgault,<sup>7</sup> Aufrere and Mathieu,<sup>8</sup> deSouza Rudge,<sup>9</sup> Massart,<sup>10</sup> Digonnet, Chenebault, and Rauehy,<sup>11</sup> Fasano,<sup>12</sup> Figueiredo,<sup>13</sup> Rouffart,<sup>14</sup> and Gregoire.<sup>15</sup>

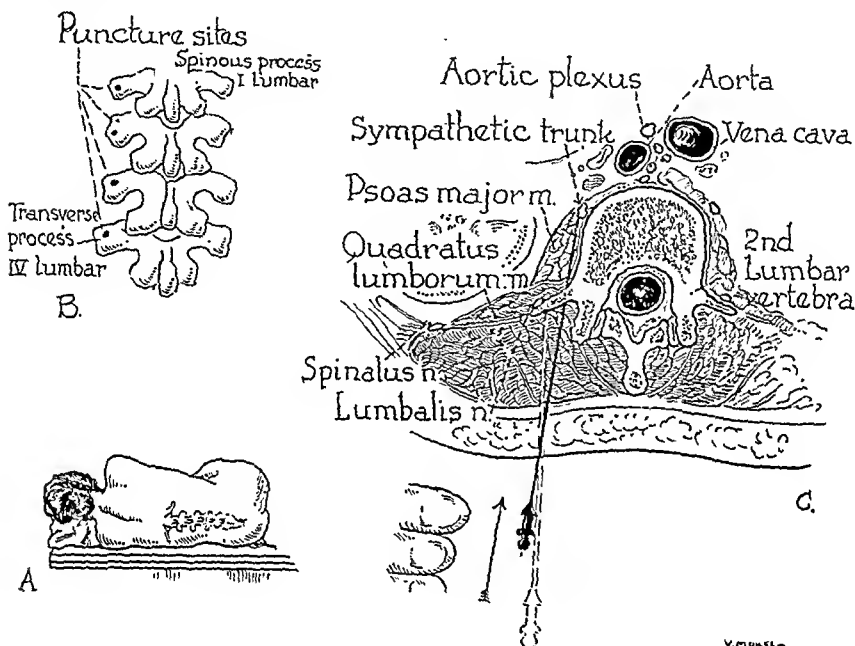


Fig. 1.—Technique of lumbar sympathetic block in thrombophlebitis of lower extremities. A, Lateral recumbent position of patient. B, Cutaneous sites of puncture lie on a horizontal level with and two and one-half fingerbreadths lateral to upper part of spinal processes of first four lumbar vertebrae. These puncture sites in the skin are immediately over the transverse processes of the respective vertebrae. C, Each needle is inserted vertically until transverse process of corresponding vertebra is reached as represented by dotted needle. Direction of needle is then changed slightly and inserted two and one-half fingerbreadths beyond the transverse process so that its point lies near the anterolateral surface of the body of the vertebra where the sympathetic chain lies.

We are in hearty agreement with the contention of Leriche that the clinical manifestations in thrombophlebitis are due largely to the vasomotor reflex which originates in the thrombosed segment, that the symptoms can be relieved completely, and that the convalescence will be materially shortened by blocking the sympathetics and thus breaking the reflex. On the basis of our experimental and clinical observations, however, we are of the opinion that the manifestations are due less to the associated venospasm than to an arteriospasm, the mechanism of which will be discussed completely in a subsequent presentation.<sup>16</sup>

We have used novocain block of the regional sympathetic ganglia in a number of cases and have obtained uniformly successful results in

every instance. A detailed analysis of these cases will be presented in another publication.<sup>16</sup> Immediately following the injection, there has been complete relief of pain which in some instances has been permanent. In others, subsequent injections have been required, but only rarely has it been necessary to use more than three injections. Within twenty-four hours the temperature declines and generally is normal within seventy-two to ninety-six hours. The associated swelling of the extremity begins to diminish within the first twenty-four to forty-eight hours and usually within a week to ten days has disappeared completely. In over one-half the cases the extremity has returned to its normal size within four days after the beginning of the treatment. In contradistinction to the prolonged convalescence following previously employed methods of therapy in which bed rest was necessary for from six to eight weeks and in which the postphlebotic manifestations persisted for a year

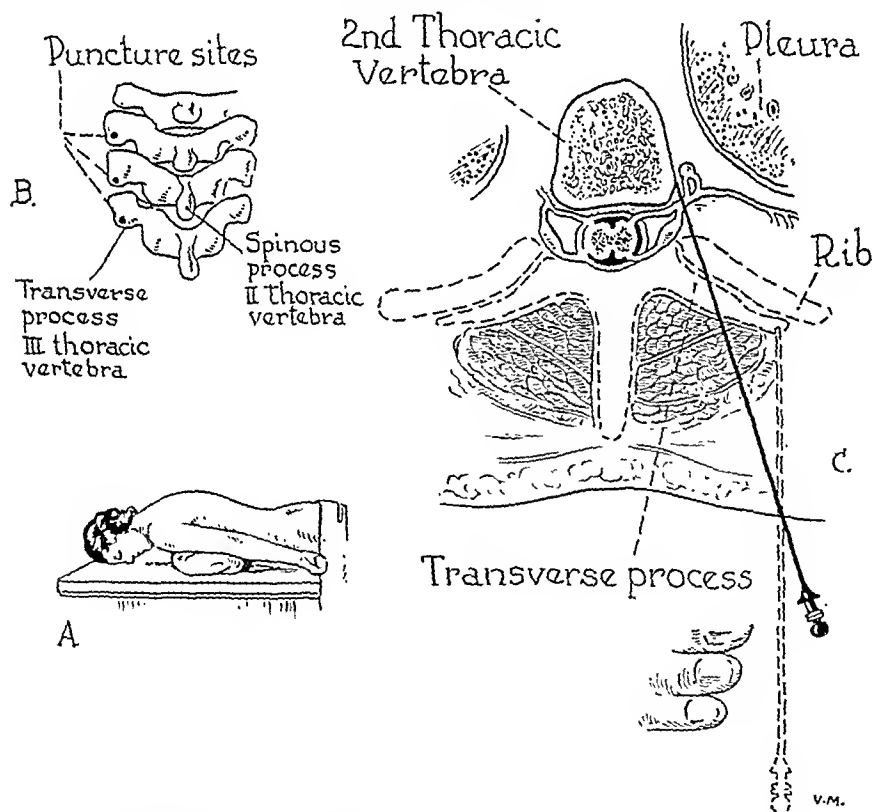


Fig. 2.—Technique of cervicodorsal sympathetic block by the posterior approach. A, Prone position of patient with pillows beneath the chest. B, Cutaneous puncture sites lie on a horizontal level with and about two and one-half fingerbreadths lateral to the spinous processes of the seventh cervical, first and second thoracic vertebrae. These puncture sites in the skin are immediately over the transverse processes of the first, second, and third thoracic vertebrae respectively. C, Each needle is inserted vertically until the transverse process of the vertebra is reached as represented by the dotted needle. Direction of needle is then changed slightly and inserted two and one-half fingerbreadths beyond the transverse process so that point of needle is near lateral surface of body of vertebra in retropleural space where sympathetic chain lies.

or longer, the patients in this group were well within two weeks and all walked out of the hospital within or shortly after that period of time. Equally as good results can be obtained in the upper extremity as in the lower, although in most instances the thrombophlebitis involves the vessels of the lower extremities, probably because of their relative inactivity postoperatively.

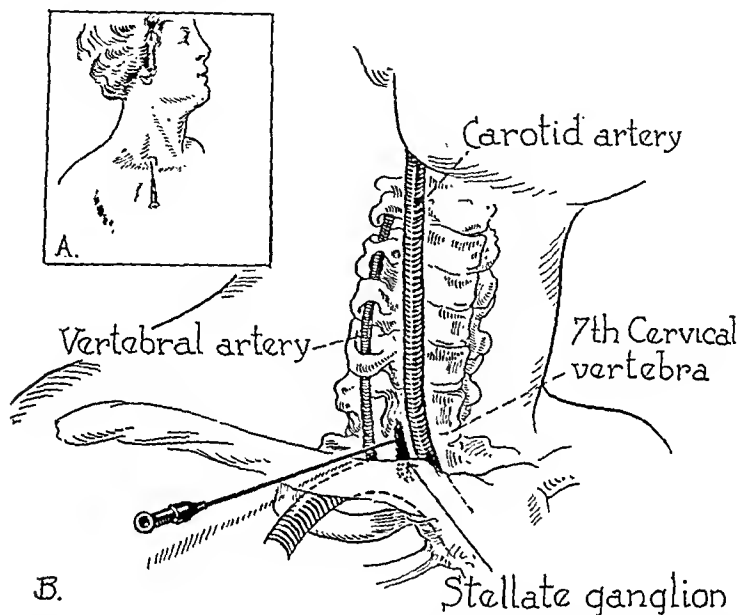


Fig. 3.—Technique of stellate ganglion block by anterior approach. A, Cutaneous site of puncture is 1 cm. medial to the midpoint of the clavicle and immediately over its upper border. B, Needle is introduced on a horizontal level with the upper border of clavicle and directed posteriorly and medially at a 45 degree angle with the midline. The point of the needle impinges against anterolateral surface of the body of the seventh cervical vertebra or at the junction between the seventh cervical and first thoracic vertebrae.

The technique of the injection of the lumbar sympathetic ganglia is extremely simple and in these cases is performed with the patient in bed. Patients with severe manifestations, in whom motion is difficult and painful, are placed in the lateral recumbent position with the affected side up (Fig. 1A). After preparation of the skin over the lumbar vertebra, wheals are made in the skin by intracutaneous injections of 1 per cent novocain at points approximately two to two and one-half fingerbreadths lateral to the upper part of the spinal processes of the first, second, third, and fourth lumbar vertebrae (Fig. 1B). These points of the skin lie immediately over the transverse processes of the corresponding vertebrae. A twenty or twenty-two gauge needle 8 to 10 cm. in length is employed. The needles are inserted vertically through each wheal until the transverse process of the corresponding vertebra is reached, usually a distance of about 4 to 5 cm. The direction of the needle is then

changed slightly either superiorly or inferiorly so that it can project beyond the process and is pointed slightly towards the midline. The needle is then inserted for another two and one-half fingerbreadths so that its point impinges against the anterolateral surface of the body of the vertebra in the retroperitoneal space (Fig. 1C). Through each of the needles, 5 c.c. of 1 per cent novocain is injected. Before injection, aspiration should be done in order to avoid the injection of novocain into a blood vessel. Within a few minutes after a satisfactory injection, the extremity on this side becomes warm and dry. Moreover, it has been our observation that the superficial veins become more prominent.

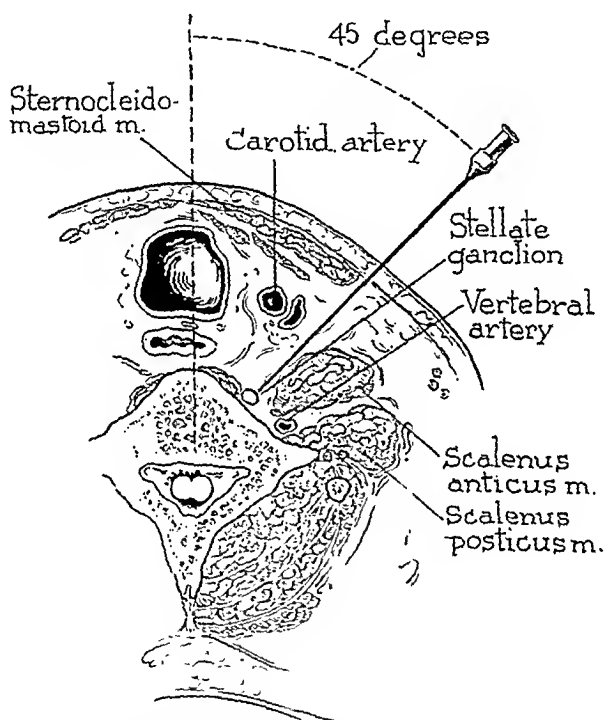


Fig. 4.—Diagrammatic drawing illustrating introduction of needle posteriorly and medially at a 45 degree angle with the midline so that the point of the needle impinges against anterolateral surface of the body of the seventh cervical vertebra or at the junction between the seventh cervical and first thoracic vertebrae where stellate ganglion lies.

We have had two cases of thrombophlebitis involving the upper extremity in which this method of therapy was used. The technique of injection of the cervicodorsal sympathetic ganglia is extremely simple. One may use either the posterior or anterior approaches. In employing the former, it is desirable to place the patient in the prone position with pillows beneath the chest (Fig. 2A). Needles similar to those used for the lumbar injection are satisfactory. Unlike the lumbar region, the spinous processes of the thoracic vertebrae are directed obliquely downward so that the end of the spinous process of each vertebra lies on a

horizontal level with the transverse process of the vertebra below. Accordingly, the cutaneous sites of injection are made approximately two and one-half fingerbreadths lateral to the spinous processes of the seventh cervical (which is the highest prominent vertebral spine), the first, second, and third thoracic spines (Fig. 2B). The needles are similarly introduced perpendicularly until the transverse process of the vertebra is reached. The direction of the needle is changed slightly as in the technique for the lumbar region so that it can slip beyond the transverse process and is directed toward the midline. It is inserted for another two and one-half fingerbreadths until the point of the needle lies on the anterolateral surface of the body of the vertebra in the retropleural space where the sympathetic trunk lies (Fig. 2C). Aspiration should always be attempted as this precaution will avoid the injection of novocain into a blood vessel or the subarachnoid space. If the point of the needle impinges directly against the vertebral body, the injection may be difficult. An attempt should be made to slip the point away from the body slightly. Five cubic centimeters of 1 per cent novocain solution is injected through each of the needles.

In injecting the stellate ganglion, we prefer the anterior approach, the technique of which is a modification of that described by Leriche.<sup>15</sup> This has the great advantage of being much simpler than the posterior approach. A point 1 cm. medial to the midpoint of the clavicle is chosen and an intracutaneous wheal of novocain is made in the skin immediately over the upper border of the clavicle (Fig. 3A). A fine lumbar puncture needle is introduced on a horizontal level with the clavicle and directed posteriorly and medially at a 45 degree angle with the midline (Figs. 3B and 4). The point of the needle, after being introduced for a distance of 6 to 7 cm., impinges against the anterolateral surface of the body of the seventh cervical vertebra or at the junction between seventh cervical and first thoracic vertebrae, where the stellate ganglion lies. After ascertaining by aspiration, that the needle is not in a vessel, 10 c.c. of 1 per cent novocain is introduced. A satisfactory injection is determined both in the anterior and posterior approaches by the presence of Horner's syndrome, anhydrosis, and increase in warmth of the extremity on the injected side.

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## SURGICAL KNOTS AND SUTURES

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WITH the rapid strides that surgery has made in the last few decades, it is not surprising that many of the more fundamental elements on which it is built have been overlooked. One of these elements, the surgical knot, has received only occasional consideration. Until recently this consideration took the form of various opinions, neglecting entirely a scientific approach to the problem.

It should be definitely stated that the present inquiry into the causes of knot failure in no way champions one type of suture material over any other. It merely points out that many knots formerly thought to be quite secure are far from reliable. The important faults and causes of failure are indicated for the more common suture materials. The much argued point of "catgut versus silk" will be left for others to discuss. Undoubtedly silk has its definite indication in surgery as does catgut. How far the general use of silk may be able to encroach on the domain of catgut remains to be seen.

This study considers only those knots which must take tension or those ligatures about blood vessels where failure may mean disaster. It in no way applies to ordinary subcutaneous bleeders. Almost any knot about these seems entirely satisfactory.

It has been our contention that the weakest part of any suture or ligature which is subjected to tension is the knot which secures the suture ends. This has been amply demonstrated.<sup>2, 3, 5</sup> It is usually assumed that the knot which the surgeon ties is inviolate. If this is so, and we strongly doubt it, then the next weakest link is that portion of the suture material immediately adjacent to the knot. At this point the suture has been sharply kinked and some of the fibers fractured by sharp turns imposed by the knot. This has been shown to provide an actual weakness as well as a theoretical one.<sup>3, 5</sup>

What are the factors which produce a stable knot? What effect has the suture material itself on the knot? What change may result when tissue fluids moisten the knot? What type of knot is the most reliable under tension? And last, of how great importance is the individual factor of the operator himself?

## GENERAL CONSIDERATIONS

A knot is defined as "the fastening made by entangling together one or more cords." Such a definition neglects the most important feature of a surgical knot. Thus for surgical purposes the above should be changed to "the fastening made by entangling together one or more cords so that any tension on the fastening causes an increased contact pressure on the component parts of the knot." An example of this ideal is found in the properly tied square knot. Here an increased tension causes the interlocking elements to bind all the more tightly upon themselves. The converse of this is any type of slip knot which has little or no tendency to increase its binding power with increased tension.

It follows then in the last analysis that a knot stays tied because of the friction of one component part upon another. If a given knot is composed of material having a high coefficient of friction, then its holding power is much greater than one tied with a slippery material having a low coefficient of friction. The coefficient of friction of a given suture material may undergo a marked alteration when it becomes moist.

Since the holding power of a knot is so largely dependent upon the friction of one suture strand upon another, it seemed desirable to determine the frictional values of various common suture materials when tied in the form of a knot. This has been done for both wet and dry sutures by a method previously reported.<sup>5</sup> The values obtained indicate a marked variation for different materials. Subsequent trials run for the present study have slightly altered the previous findings. However, the general ratios remain unchanged. These revised wet and dry coefficient of friction values are given in Table I. Their significance will be commented upon later.

TABLE I  
COEFFICIENT OF FRICTION VALUES\*

	DRY	WET
Silkworm gut	0.15	0.14
Dermal	0.15	0.15
Silk (serum proofed)	0.18	0.17
Silk (moderate wax impregnation)	0.29	0.33
Silk	0.18	0.32
Linen	0.22	0.40
Catgut, plain	0.18	0.29
Catgut, chromic	0.19	0.35

\*These are average values. The smaller sized material gave somewhat lower values than the larger. Saline was used to moisten the sutures since the results obtained were practically the same as when using animal serum.

There are certain factors and conditions peculiar to suture material which definitely alter the holding power of a knot. Briefly these are:

1. *Moisture*.—It is common knowledge among musicians that the gut of stringed instruments is apt to snap or the knots come untied during damp weather. It is likewise known by surgeons that catgut seems to be more slippery wet than dry and that knots tied with wet gut have a great tendency to slip out. What is the reason for this physical change?

It was assumed that the moisture caused a decrease in coefficient of friction, thus allowing the knot to slide. This assumption proved to be totally false, as is shown in Table I. Here it is seen that the wet frictional values were nearly double those of the dry catgut. As might be expected, those materials, such as dermal or serum-proofed silk, which are impervious to moisture showed practically no change in the wet state over the dry. On the other hand, materials, such as ordinary silk and linen, which absorb considerable quantities of moisture nearly doubled in their frictional values. Why then is it that, though the values are high for wet catgut, a knot tied with this material has such a great tendency to fail?

There are two very logical explanations for this. First, as a strand of dry catgut picks up moisture it assumes a quality it did not formerly possess; namely, that of elasticity. This should better be termed elongation since once the strand is stretched there is only little tendency for it to return to its former length. Thus it is seen (Table II) that a strand of dehydrated plain catgut stretches but about 1 per cent under a tension of 1 kg. After the same strand has been immersed in saline solution for a few minutes, it will elongate 14 per cent under the same tension.

TABLE II

EFFECT OF MOISTURE ON CATGUT ELASTICITY AND SIZE. AVERAGE VALUES

	% STRETCH DRY 1 KG. TENSION	% STRETCH WET 1 KG. TENSION	% DIAMETER INCREASE WET
No. 1 plain boilable	1.2	14.0	55
No. 1 chromic boilable	1.2	8.0	50
No. 1 plain nonboilable	8.5	11.0	18
No. 1 chromic nonboilable	6.5	8.0	20
Linen	0.7	1.8	-

This quality of wet catgut has a very definite bearing on the holding power of a knot. It prevents the tying of a hard firm knot. Also when tension is put on such a knot its component parts have a tendency to roll over each other until the cut suture ends finally roll out. Much the same action is noted when two ends of a rubber band are tied together and then subjected to tension. The knot merely rolls out.

Another factor in the failure of catgut knots is the swelling of the material itself as it takes up moisture. It will be seen (Table II, Fig. 1) that the diameter of a strand may increase half again its original size. Of course, this has a very definite tendency to swell the knot loose.

It is obvious that in material such as dermal or serum-proofed silk the quality of the strand is not altered by moisture. Therefore, the ability of the knot to hold remains unchanged.

2. *Local Flaws and Suture Irregularities.*—Regardless of the material used, there may always be a few irregularities or flaws at the site of the knot. At times these tend to catch and hold the knot throws more firmly.

At other times they may prevent the throws from lying flat or from coming tightly together. Again, the sharp turns necessitated by the knot may actually fracture the suture material.

The size of the suture material may also affect the holding power of the knot. The knot throws of the larger sizes often cannot be brought tightly together because of their actual bulk or because of their stiffness. This is an argument in favor of small sized suture. For, if a suture is only as

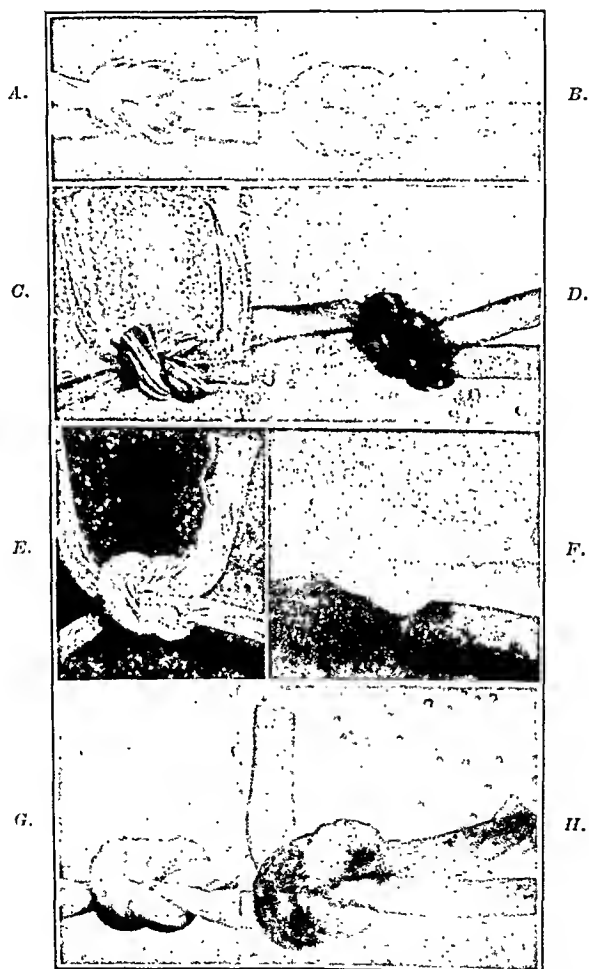


FIG. 1.—Illustrating changes taking place in catgut square knots subjected to moisture. All photographs are exactly the same magnification. *A*, Nonbollable plain catgut. *B*, Same knot after 45 minutes' immersion in normal saline. Note definite swelling of strands and tendency to "swell loose." *C*, Nonbollable chronic catgut. *D*, Same knot after 35 minutes' immersion in 10 per cent pepsin solution. Moderate swelling is evident but knot still appears firm. *E*, Nonbollable plain catgut which was allowed to dry in the air for an hour before tying the knot, thus allowing some of its originally contained moisture to evaporate. *F*, Same knot after 35 minutes' immersion in normal saline. Note marked swelling of strands which has caused the knot to "swell loose," making it absolutely untrustworthy. *G*, Bollable plain catgut. *H*, Same dehydrated gut absorbs water. An unreliable knot is the result, and the short ends easily roll out.

strong as its weakest link (the knot), there seems no advantage in using a heavy material whose knot is no stronger than that of a much smaller size.

3. *Personal Factor*.—Much has been said and written<sup>4</sup> about the personal element in tying knots. It is agreed that there is a great deal of difference in knots tied by different operators. However, this does not tell the entire story. The above should be amended to "there is a great difference in knots tied by different operators and a vast difference in knots tied by the same operator."

It was a revelation to the writer to find that some of his knots came untied, not those placed on subcutaneous bleeders but knots of sutures on fascia which were tied to stay tied. It was this experience which led to the present study.

The surgeon naturally feels that others may tie faulty knots but that his knots are beyond reproach. We say naturally, since if he did not have this conviction he would change his methods. To those who are certain that they can tie a square or "surgeon's" knot which is trustworthy, the following is suggested: Tie one of the above knots with a strand of plain, nonboilable catgut which has been moistened with saline solution or serum. Tie this as would be done while operating, one-handed or two-handed, and cut the ends as usual. Then subject the knot to tension. We have yet to see such a knot hold to the point of breaking. It merely rolls out. Nearly the same may be said of the highly waxed, serum-proofed silk. It is obvious then that the square or "surgeon's" knot is entirely inadequate when dealing with these suture materials. What knot then may be safely used?

4. *Type of Knot*.—In comparing the holding power of different knots, it is imperative to reduce the number of variables to a minimum. This was done in a knot testing apparatus previously described.<sup>5</sup> No attempt will be made here to describe this method other than to state it consists of a means by which a series of knots can be subjected to an intermittent stress of two and one-half pounds. This tension is considerably more than the usual knot is required to stand but is certainly not out of the realm of possibility.

Further tests were carried out along the line previously detailed. One variation was made in that a known tension was used in tying the knot. This was done by means of a spring scale attached to one of the suture ends. The tying tension varied from one and one-half to five pounds but was always kept the same for a given series of trials. The results obtained were practically the same as those previously reported. In brief these are as follows:

A carefully made square knot is reliable when tied with ordinary silk or linen. When boilable plain or chromic catgut is used, such a knot holds fairly well, though it is by no means absolutely reliable. But, this same

catgut knot becomes completely untrustworthy if immersed in saline solution or serum for a time before testing so that it swells and becomes capable of stretching as previously noted. The same may be said of the nonboilable type of catgut. In the plain type of this material we have never been able to tie a square knot which will hold if tied wet and in the manner used in making ties under operative conditions. The chromicized catgut has a definitely greater holding power.

Square knots tied with serum-proofed (waxed) silk were found to be quite unreliable. This will be discussed later.

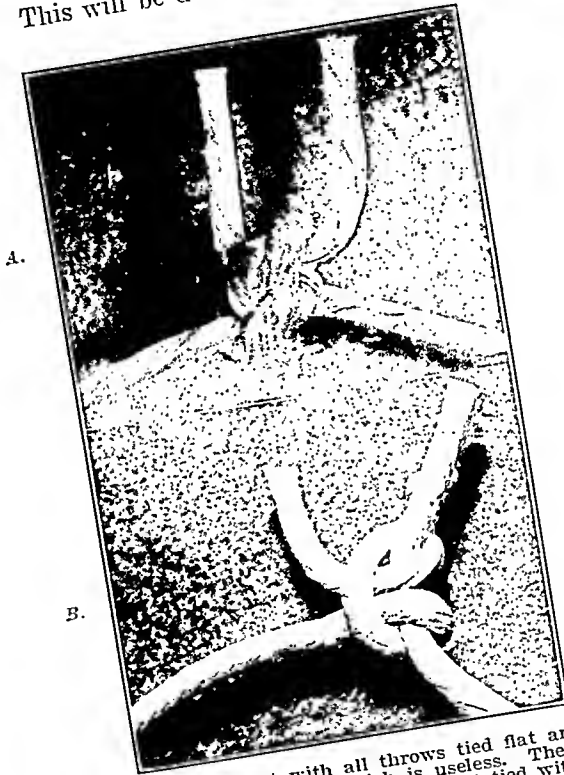


Fig. 2.—A, A triple throw knot with all throws tied flat and square is the safest of all simple knots. B, A square knot which is useless. The throws have not been pulled flat. This is frequently the type of square knot tied with one hand where care is not taken to cross the hands between throws and exert equal tension on each strand. Unfortunately it also occurs when extreme care is given to this particular fault.

When testing the surgeon's knot, it was quite surprising to find that this knot was definitely less reliable than the square knot. It was found that, unless the second throw causes the first to overlap upon itself and thus set the knot, there was a very definite tendency to give way due to the components not coming firmly in contact. The surgeon's knot is often desirable to use since the extra lap on the first throw helps hold the tension until a second throw can be placed. When this is the case, a third throw is imperative to make the knot reliable.

As to the relation of the suture material to the surgeon's knot, it is much the same as that indicated in the previous paragraphs.

strong as its weakest link (the knot), there seems no advantage in using a heavy material whose knot is no stronger than that of a much smaller size.

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Fig. 4 indicates faults in the knot securing the ends of a continuous suture. It will be noted that in Fig. 4 A the actual bulk of the knot prevents the two throws from coming tightly together, giving a knot which easily slips out. Fig. 4 B again emphasizes the difficulty of obtaining a flat square knot when one component of the knot is less pliable than the other. Here the bulk and stiffness of the two suture strands is too great to interweave with the single strand. The result is the indicated knot which is perfectly useless.

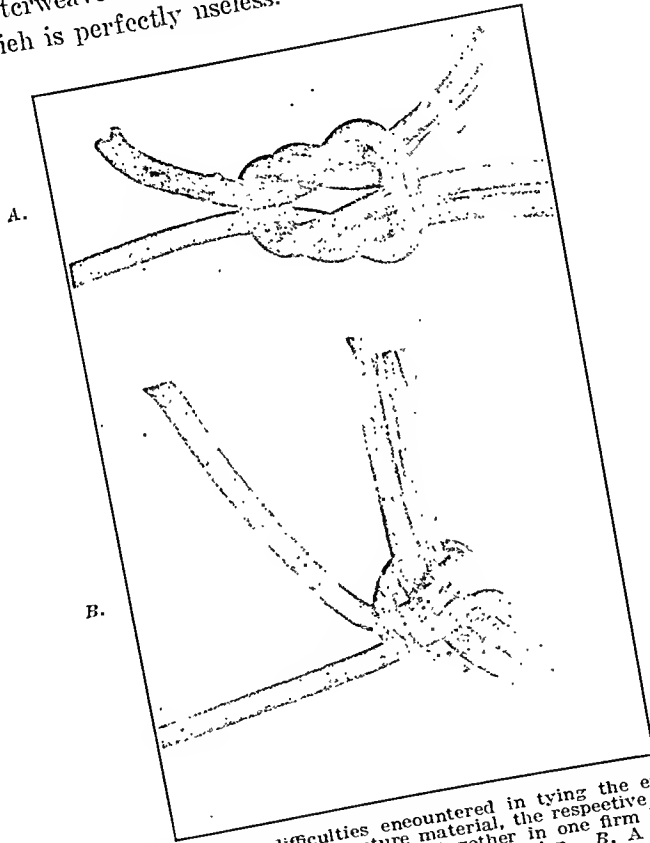


Fig. 4.—Illustrating the difficulties encountered in tying the ends of a continuous suture. A, With the larger sizes of suture material, the respective throws are extremely bulky. It is difficult to pull them down together in one firm knot so that the cut end of the single strand will not slip out under tension. B, A too frequent type of square knot encountered in fastening a continuous suture. Its cause is obvious—tension on the two strands while tying with one hand and the bulk of the two strands which prevent them from interweaving with the single strand so as to form a flat square knot.

Trial tests of square knots tied with three strands, as when completing a continuous suture, show them to be completely untrustworthy. In fact, we were shocked by the large number of failures which occurred even when a triple throw knot was used. If the suture material consisted of wet catgut or waxed silk, the only knot which was completely reliable was a quadruple throw knot. It is therefore strongly advocated that a quadruple throw knot be used when fastening the ends of a con-



A triple throw knot is the safest of all simple knots. To all practical purposes it is trustworthy for all suture materials with the occasional exception of wet plain catgut. It is of course safest when all throws are tied square (Fig. 2), but it is fairly reliable when two of the throws are square.

A few other factors entering into an analysis of the knot itself are indicated in Figs. 2 and 4. These are photographs of rather large size catgut. Obviously the errors indicated might occur with any suture.

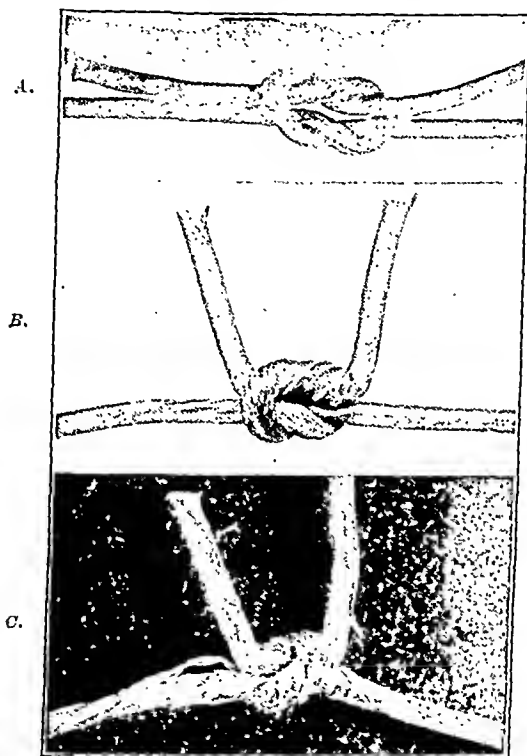


Fig. 3.—A, Square knot tied with heavy chromic boillable catgut. This material is too "wiry" to be pulled down into a firm knot. The throws spring apart as indicated. B, Hard firm square knot showing early fracture of fibers composing the knot. C, A firm square knot which will not slip, but fibers of the catgut strand have been badly fractured in the tying. This produces an extremely weak area immediately adjacent to the knot.

although they might be expected less frequently with smaller and more pliable material. Fig. 2 indicates a square knot which is absolutely useless since the throws have not been pulled flat. This is frequently the type of square knot tied with one hand where care is not taken to cross the hands between throws and exert equal tension on each side. Unfortunately it also occurs even when extreme care is given to this particular fault and when one strand is less pliable than the other, thus preventing the desired interlocking.

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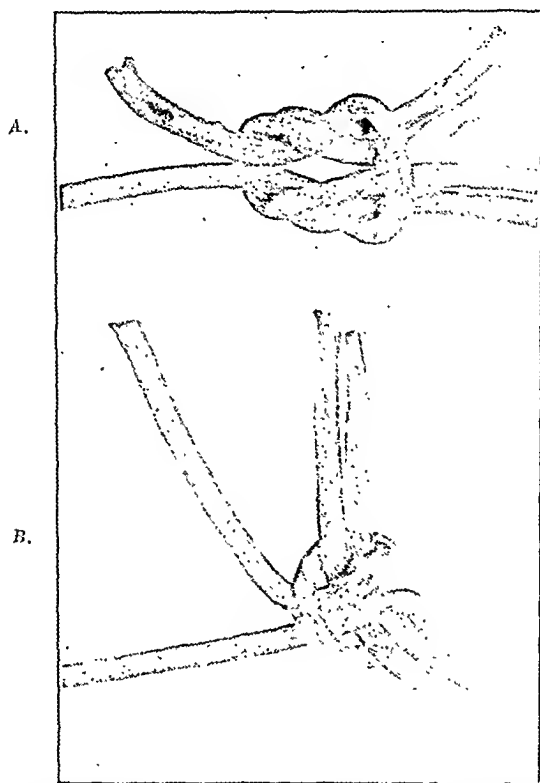


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tinuous suture which must take tension. Since the start of a continuous suture consists of only single strands, a carefully tied triple throw knot should suffice.

The above procedure demands that an unusually large amount of suture material be buried in the tissue. This would seem to be safer than taking a chance on a lesser amount and a knot which might prove untrustworthy.

5. *Length of Cut Suture Ends.*—The length of the cut ends of a knot is also an important factor in knot failure. Often the throws of a knot which is subjected to stress will reseal themselves after rolling over each other. After reseating, a good firm knot may result. This is frequently the case with silk treated with the wax compound. Therefore, if the

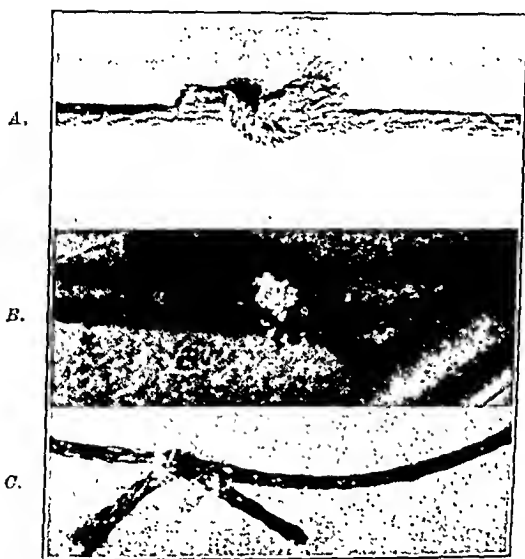


Fig. 5.—A, Firm square knot tied with serum-proofed black silk. The knot has slipped to its present position, scraping off the wax used to impregnate the silk. The white wax can be seen collected about the knot. B, Same as above with larger strand of black silk. The wax has the effect of a lubricant decreasing the coefficient of friction value of the silk strand. C, Square knot of silk with ends cut very short. Any slipping or rolling of the knot would allow the ends to pull out.

suture ends are not sufficiently long to allow for this slight slipping, the knot may quite easily fail. Fig. 5 C indicates such a situation. It is obvious that any further slipping of this knot would allow it to come untied.

Long cut ends, of course, are undesirable since they add to the amount of foreign body left in the tissues. However, when safety of the knot is important, the longer ends must be tolerated. It would seem from our experience in this phase that catgut suture ends should be left at least 6 mm. long. For smaller sizes of silk this might be reduced to 3 mm.

It is the custom of some operators using black silk on small bleeders to tie a triple throw knot and then cut the suture ends right down on

the knot. This seems a perfectly sound practice for the situation indicated. However, it is apt to give the operator a false sense of security in its use at other sites. The third throw of a knot so cut usually comes loose and most certainly would if subjected to any tension.

There are certain features of knots tied with catgut and with silk which should be considered separately. These two materials are by far the most frequently used prototypes representing the general groups of absorbable and nonabsorbable sutures.

#### CATGUT

The boilable type of catgut is a dehydrated form. It is wiry and stiff. Carefully tied knots of this material are fairly secure when tied dry. In the conditions of our tests they held in a high percentage of instances. This was true when using the "surgeon's" or square knot. No doubt it is because of this, that so much faith has been placed in simple knots. But, though the suture may be used in its dehydrated form, it rapidly picks up moisture from the tissues and then closely resembles the nonboilable hydrated type of catgut.

This change is inevitable and as pointed out causes a vast change in the physical structure of the strand. It swells (Fig. 1, Table II); it elongates easily with tension; it tends to untwist; and last, contrary to usual belief, there is a marked increase in the frictional values of one strand upon the other. All of these factors, with the exception of the last mentioned, have a tendency to weaken the holding power of the knot.

The softer, more pliable, nonboilable (partially hydrated) catgut has these objectionable features to start with, so at least it does not give the operator a false sense of security. However, the simple knots tied with this material are quite untrustworthy.

We must then face the fact that simple knots tied with any type of catgut are untrustworthy. Since this material enjoys nearly universal use, it is obvious that we must fit our practices to the limitations of the catgut. It is therefore advocated that at least a triple throw knot be used in fastening two suture ends. Where three strands enter the knot, as at the end of a continuous suture (Fig. 4), a quadruple throw must be used.

Again it should be emphasized that this does not apply to the usual small bleeder but only to use at sites where a suture takes tension. In this connection it may be stated that we are convinced that only very few sutures are ever subjected to the tension used in our tests (two and one-half pounds). If they were, there certainly would be far more abdominal wall failures following laparotomy. It then follows that, if this is the case, why use the large size catgut which is such common practice? Certainly a smaller size would be ample if care were taken not to break it by the shearing action of tying the knot. The size of catgut seems to make little difference in absorption time of the material.<sup>1</sup> Therefore,

it would appear that much of the tissue reaction produced by catgut would disappear if fine sizes of catgut were more generally used.

One more point should be mentioned. Knots tied of chromic material are definitely more secure than those tied with plain catgut. It is not known if this is due to the high frictional value of chromic (Table I) or to its lesser degree of stretch under tension. We are inclined to believe it is the latter.

#### SILK

In a previous report the statement was made that knots tied with silk were much more reliable than those tied with gut.<sup>5</sup> This is true when dealing with the ordinary untreated type of surgical silk. It is not true for the waxed type of serum-proofed silk. This material was referred to in the previous communication as "hard twist silk."

Serum-proofed silk consists of a high quality braided silk strand which has been impregnated with a wax compound. This combination gives a suture material of many desirable qualities. It is extremely strong so that very fine sizes may be used, thus minimizing the amount of nonabsorbable foreign body left in the tissues. It is practically moisture proof and therefore does not change its physical properties on contact with tissue fluids. It at least diminishes the danger of wound infection by being moisture proof, thus reducing the opportunity of harboring bacteria. Last, probably its most desirable quality from a practical standpoint is that it may be boiled or autoclaved without fear of lowering its tensile strength.

From the standpoint of knot safety, the serum-proofed silk has one very definite objection. The wax which coats the strand prevents moisture from aiding in making a firm knot as with ordinary silk. This lubricating action of the wax allows the knot to slip on itself, and the cut ends may slide out (Fig. 5). It will be noted (Table I) that there is no increase in wet friction value over dry.

This feature of serum-proof silk at times is not altogether a fault as it allows the operator to slide the second throw of a knot, thus holding it until a third throw can be applied. At the other extreme are suture materials, such as untreated wet silk or linen, which have a very high coefficient of friction. The friction of one strand of the knot upon another may be so great that the suture breaks before it can be pulled down snugly. This is commonly experienced when using linen or ordinary silk in pulling down the first throw of a surgeon's knot. Once the knot is carefully and securely tied, these materials produce the safest of all knots.

During our tests, there was occasion to examine some braided silk which was lightly impregnated with a wax compound. Knots tied with this material wet or dry were extremely reliable. This was in sharp contrast with square knots tied with the full impregnation of the serum-proofed silk.

From the foregoing it would seem that a more desirable material would be one which contained less wax than the full serum-proofed silk. Boiling removes some of this wax. A single such sterilization, however, does not remove enough to greatly alter the holding power of the knot.

A desirable property which nonabsorbable suture seems to possess is that it elongates very slightly under tension. This is true wet or dry. The knot never fails, due to a stretching out of the suture, as is the case with catgut.

#### DISCUSSION

It has not been our purpose to uphold one type of suture as being ideal either as a suture or for the safety of its knots. To our knowledge there is no such ideal material. Rather has it been our purpose to indicate the frailties and faults of all simple surgical knots. An analysis of these faults and causes for knot failure is given in detail. It is pointed out that special care and consideration must be given to knots tied with the suture material at our disposal. If this is not done, there will be a considerable number of failures in those knots which are subjected to tension.

A few generalities may be stated.

1. A knot is the weakest point in any suture. If the knot itself holds, then the portion of the suture immediately adjacent to it becomes the weakest link.

2. Square knots and "surgeon's" knots are unreliable for tension sutures when using catgut or serum-proof (waxed) silk. Chromic catgut knots are somewhat more reliable than those of plain catgut. The latter foots the list.

3. Failure of catgut knots is largely due to the change in physical properties on becoming moistened by tissue fluids.

4. Failure of the waxed silk knots is largely due to the fact that the wax acts as a lubricant, allowing the knot to slip.

5. A tension suture often slips slightly and then holds. This indicates the importance of leaving long cut ends on the knot.

6. Linen and untreated silk are the safest materials in so far as the knot is concerned.

7. Due to the limitations of the available suture material and the personal element of the operator himself, particular caution must be taken with all knots subject to stress.

8. It is advised that a carefully tied triple throw knot be used with the throws all tied square.

9. Where three strands of suture are tied together, as at the end of a continuous suture, a quadruple throw knot is recommended.

10. In our tests the "surgeon's" knot was consistently less reliable than the square knot. It demands a third throw to make it safe.

It is interesting to reflect upon the past, present, and future of sutures and their knots. We still approximate tissues in the same manner that they were first approximated in early medical history, using for the most part the same type of suture and the same knots as our early medical ancestors. We have added little to their methods with the exception of sterile technique. Will the future develop a method of better holding tissues together while they repair than the one which antiquity has passed down to us? Or, will we continue to sew and tie knots hoping that eventually the perfect suture will be developed, a suture which is nonprotein, perhaps closely allied to a cellulose, nonelastic, slowly dissolvable in tissue fluids, and capable of being tied in simple knots which are absolutely trustworthy? In the meantime, a knot is still the weakest part of any suture.

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# A STUDY OF THE USE OF SILK, CATGUT, AND THE NOBLE PLICATION WITH REFERENCE TO ABDOMINAL ADHESIONS

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THE predisposition to morbidity which may arise from the injudicious use of suture materials seems insufficiently appreciated. The results reported here are based upon 152 autopsies and operations upon 76 animals (dogs). Our observations in this series of experiments, together with previous investigations of similar nature,<sup>1,2</sup> have made us keenly conscious of the fact that every surgeon should be thoroughly familiar with tissue reactions and potential complications which may arise with various suture materials.

A detailed analysis of the literature on this subject will not be given here. Findings which have been made to date by studies on silk and catgut should be briefly stated in general, however. A number of investigators during the past few years have demonstrated considerable variability in the grades and types of catgut sutures which are marketed by different companies, and also some variability of catgut sutures marketed by the same companies. It is accepted that the sterility problem in the preparation of catgut is a considerable one. Chemical methods commonly used apparently are not completely efficacious in killing spores of certain anaerobic microorganisms, such as *Cl. welchii*, or of always killing all unspored microorganisms. Heat seems to be the only sure sterilizing agent available at present in suture manufacture; and many surgeons do not favor boilable catgut because of its increased hardness and lessened pliability. Chemical agents, such as chromic acid and iodine, used in chromicizing or tanning catgut are in themselves irritating to the tissues. Even plain catgut seems to cause a certain amount of inflammation and edema of the tissues as it is absorbed. Allergic reactions to catgut with consequent disruption of wounds likewise have been demonstrated.

One of the chief objections to the wider use of silk seems to have been that it is a nonabsorbable material. It has also been a prevalent belief that silk should never be used in a field involved in or threatened by pyogenic infection. Many objections to the use of silk seem to have been accepted more upon theory than upon actual experimental or clinical facts. The extent to which Halsted popularized the use of silk and stipulations which he and others made regarding its use are well known. Halsted, however, seemingly did little actual experimental work with silk.



It is interesting to reflect upon the past, present, and future of sutures and their knots. We still approximate tissues in the same manner that they were first approximated in early medical history, using for the most part the same type of suture and the same knots as our early medical ancestors. We have added little to their methods with the exception of sterile technique. Will the future develop a method of better holding tissues together while they repair than the one which antiquity has passed down to us? Or, will we continue to sew and tie knots hoping that eventually the perfect suture will be developed, a suture which is nonprotein, perhaps closely allied to a cellulose, nonelastic, slowly dissolvable in tissue fluids, and capable of being tied in simple knots which are absolutely trustworthy? In the meantime, a knot is still the weakest part of any suture.

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silks, and unquestionably it has a definite place in the surgical armamentarium. It occurred to us, however, that, just as the treatment of catgut with irritating chemicals may predispose to inflammatory tissue reaction, so special treatment of silk, unless carefully guarded, might likewise make the product more irritating to tissue than it otherwise would be. We therefore do sound a note of warning concomitant with the increasing popularity of the silk suture. Its increasing popularity undoubtedly will call for increased activity regarding it on the part of commercial houses. And it is entirely possible that more and more supply houses will bring out "specially treated" silks.

We are not familiar with any extensive well-controlled experiments which have carefully measured reactions or complications which might arise from the use of specially prepared silks in the peritoneal cavity. We therefore decided to continue experimental investigations comparing two or three types of silk as well as catgut.

TABLE I  
CATGUT 20-DAY NONBOILABLE CHROMIC 0 ON INTESTINAL NEEDLE

DOG NUMBER	DATE OPERATED	DATE AUTOPSIED	ADHESION GRADE*	REMARKS
SS-D7	3/ 4/38	4/29/38	0	Part of gut strand unabsorbed (figs. 1 and 2)
SS-D11	3/14/38	5/17/38	Grade 1	Band omentum to knot area only
SS-D15	7/ 1/38	7/24/38	Grade 3	Bowel, omentum involved
SS-D16	7/ 2/38	7/24/38	Grade 2	Grade 2 omental adhesion along suture line and to mesentery
SS-D17	7/ 2/38	7/24/38	Grade 3+	Omental adhesion all along suture line; one extra knot in suture
SS-D18	7/ 4/38	7/24/38	Grade 3	Adhesions loop to bladder, etc.; a good experiment; photograph
SS-D19	7/ 4/38	7/24/38	Grade 1	Omental strand to knot area; no adhesions elsewhere
SS-D20	7/ 5/38	7/29/38	Grade 2	Omental adhesions to greater part of suture line
SS-D21	7/ 5/38	7/29/38	Grade 1	Knot region to abdominal wall; none elsewhere
SS-D22	7/ 6/38	7/29/38	Grade 2	Omental adhesions over three-fourths of suture line
SS-D23	7/ 9/38	7/29/38	Grade 1½	Loop of bowel to suture line
SS-D24	7/ 9/38	8/ 3/38	Grade 3-	Bowel to self and omental adhesions; more trauma at operation
SS-D25	7/25/38	8/25/38	Grade 2+	Omentum along suture line
SS-D26	7/29/38	8/25/38	Grade 1+	Heavy strand to knot region; none elsewhere
SS-D30	8/ 4/38	8/25/38	Grade 2	Omentum to one-half of suture line; no pus on dissection suture line
SS-D31	8/ 4/38	8/25/38	Grade 2	Omentum to suture line; no pus on dissection
SS-D34	8/25/38	8/28/38	Grade 2	Dog died, cause unknown; Grade 2 adhesions probably would have been permanent

\*Grade 1 or less, 4; Grade 2 or more, 11; Grade 3 or more, 3; Grade between 1 and 2, 2; Grade 2, 6; total number observed, 17.

Shambaugh and Dunphy recently did investigative work which indicated that silk could be used in the presence of infection;<sup>8</sup> that actually there seemed less tissue reaction and undesirable sequelae following its use in their studies than following the use of catgut. This, of course, directly contradicts popular and long-standing belief.

Harvey, in a recent editorial, advocated the use of silk in resections of the colon in cases where greater pliability of silk would make for more secure closures than would be available with less pliable catgut.

Men in several well-known medical centers are looking with more and more favor upon the use of silk as a satisfactory material to be buried in tissues. Particularly at Johns Hopkins and Tulane Universities have surgeons had considerable experience with silk. At Tulane University practically the entire surgical staff is now using silk exclusively in the abdominal wall proper and also extensively inside the peritoneal cavity. Ochsner, however, warns against the use of long continuous strands of silk in closure of the abdominal wall, stressing the interrupted suture. Gage frequently uses ordinary ten-cent-store white cotton thread, size 50-60, in both the abdominal wall and in the peritoneal cavity. Whipple, of New York City, apparently uses continuous silk sutures in closure of the peritoneum.<sup>9</sup>

Schindler has demonstrated that silk strands used in the wall of a viscus, before they are absorbed, may possibly present free ends waving in the hollow viscus. Free ends were found by Schindler in the stomach following gastroenterostomies. He stated that at such sites in a hollow viscus irritation may occur.<sup>6</sup> We are not familiar with just how complete and voluminous his observations regarding this point are.

Since we had on occasions used the Noble plication technique for prevention and treatment of abdominal adhesions and had previously wondered which would be preferable suture material in this procedure, we decided to do experimental plications on dogs with continuous silk and catgut strands, and to pursue the fate of the sutures over periods of time. Some of our previous experiments had led us to look with increasing favor upon the use of silk.<sup>1, 2</sup>

Certain manufacturers are specially treating and preparing silk and have made claims that their method of treatment develops a silk considerably superior to untreated silk. One of the most popular silks is claimed to be made moisture and serum proof by the manner in which it is treated. It is treated with a mineral wax and "processed in such a manner that each strand is impregnated and the entire surface covered." "It does not irritate and has no allergic reaction" according to the claims of the manufacturer. Another statement made in advertisements of the product is: "It has no chemical or allergic reaction and is non-irritating—eliminating the possibility of suppuration." It must be admitted that this particular brand of silk is stronger than most other

physiologic function of the involved loops; or if the procedure could predispose in any manner to mechanical stasis or obstruction at the curve of the plication. We may say here that we found no evidence in our experiments indicating that such disturbances occurred.



Fig. 1.



Fig. 2.

Figs. 1 and 2.—These two photographs illustrate the end-result which Noble attempts to achieve when he plicates the bowel upon itself to cover raw surfaces on the bowel wall which otherwise would form promiscuous adhesions. In these particular instances there was absolutely no sign of adhesion formation along the suture lines of the plicated loops. The percentage and degree of adhesion formation with various materials are listed in the accompanying tables.

## THE NOBLE PLICATION AND EXPERIMENTAL TECHNIQUE

In 1937 Noble described a technique which he used at times for prophylaxis and treatment of abdominal adhesions.<sup>5</sup> It seemed to us that the mechanical principles of the technique were of value. Briefly stated, one may simply fold a loop of bowel upon itself when by doing so one may cover abraded areas of the involved loop. Noble reasoned that by doing this and attaching by continuous suture the two loop surfaces together, one would prevent the formation of dangerous bands or unsatisfactory visceral attachments to raw surfaces (Fig. 1). The procedure is indicated, of course, only when raw surfaces cannot be more easily and satisfactorily obliterated. In making the plication, he also sutured the mesentery of the plicated loop together from its base upward to the level of the beginning of the bowel plication proper. This avoided leaving a mesenteric pocket in which loops of bowel might have strangulated themselves.

One might wonder if the attachment of the gut to itself in the manner described by Noble would in any way disturb the normal peristaltic or

TABLE II  
DEPARTMENT STORE SILK (SIZE 1)

DOG NUMBER	DATE OPERATED	DATE OF READING	ADHESION GRADE*	REMARKS
S7-D1	11/ 1/37	12/ 5/37	Grade 1	Adhesions confined to exposed knot
S7-D3	11/ 3/37	11/20/37	Grade 1	Adhesions confined to exposed knot
S7-D4	11/ 3/37	11/22/37	Grade 1	Adhesions confined to exposed knot
S7-D6	11/ 7/37	1/20/38	Grade 1	Adhesions confined to exposed knot
S7-D7	11/ 7/37	11/20/37	Grade 1	Adhesions confined to exposed knot
S7-D8	11/12/37	12/15/37	Grade 1	Adhesions confined to exposed knot
S7-D10	11/13/37	11/28/37	Grade 1 plus	
S7-D11	11/13/37	11/29/37	0	
S7-D12	11/23/37	12/25/37	Grade 1	Few omental strands suture line
S7-D13	11/24/37	12/ 6/37	Grade 3½	Many adhesions to involved loop; cause unknown
SS-D1	2/12/38	4/25/38	Grade 1	To knot area only; silk seemed inert in tissue; no pus
SS-D2	2/13/38	5/17/38	Grade 2	Gut traumatized more than usual at original operation; silk slowly absorbing
SS-D3	2/13/38	5/17/38	Grade 1 plus	To knot area and ½ inch adjacent; none elsewhere
SS-D4	2/14/38	3/29/38	Grade 1-	None on suture line proper
SS-D5	2/14/38	5/17/38	Grade 1-	Thin strand to knot area only; silk slowly absorbing
SS-D6	3/ 4/38	4/29/38	Grade 1½	Flimsy adhesions knot area and adjacent
SS-D8	3/11/38	4/26/38	Grade 1-	Small band to knot area only
SS-D10	3/14/38	5/17/38	Grade 1	Thin band omentum to knot region; none elsewhere
SS-D14	3/18/38	5/17/38	Grade 2	Lacerated serosa; predicted adhesions at original operation

\*Grade less than 1, 4; Grade 1 or less, 13; Grade 2 or more, 2; Grade 3 or more, 1; Grade between 1 and 2, 3; no adhesion, 1; total number observed, 19.

physiologic function of the involved loops; or if the procedure could predispose in any manner to mechanical stasis or obstruction at the curve of the plication. We may say here that we found no evidence in our experiments indicating that such disturbances occurred.



Fig. 1.



Fig. 2.

Figs. 1 and 2.—These two photographs illustrate the end-result which Noble attempts to achieve when he plicates the bowel upon itself to cover raw surfaces on the bowel wall which otherwise would form promiscuous adhesions. In these particular instances there was absolutely no sign of adhesion formation along the suture lines of the plicated loops. The percentage and degree of adhesion formation with various materials are listed in the accompanying tables.

In doing the Noble plication on our experimental animals, we used silk alone in some, always choosing the area of the ileum beginning at its terminal portion about three to five inches from the ileocecal junction and plicating upward. Catgut alone was used in other animals in the same areas. In some, catgut was used to plicate one area of the small gut and silk was used in the same animal for another area of plication. Plications involving as much as twenty-four inches of the small gut were done, the average length involved being about twelve inches. Twenty-day chromic 0 nonboilable catgut on an intestinal needle was used in most instances where catgut was utilized in the plications; twenty-day chromic 00 nonboilable catgut on an intestinal needle was used in other animals. Ordinary black sewing silk essentially equivalent to Size 1



Fig. 3.—This photograph illustrates two points. First, there were no adhesions of adjacent viscera or omentum anywhere along the silk suture line which was used in this plication. There has been some pulling apart, however, along one or two areas of the suture line. This is likely to happen unless the two serosal surfaces are approximated quite snugly with the suture.

surgical silk, purchased at a department store counter, was used at other times. A specially treated popular surgical silk in Sizes 1 and 2 which we will call Brand A was used; and a softer, more pliable surgical silk, Size 2, free from waxed treatment, was also utilized. Animals were killed and readings made, as a rule, in four weeks to two months. A few readings were made sooner and some later. The results are catalogued in Tables I-VII. All readings were carefully and unbiasedly made; and sufficient latitude was allowed between grade classifications to make unintentional distortion of readings seem unlikely. With the reading of Grade 1, only a minimal amount of adhesions was present, such as a thin strand of omentum over a limited area. For Grade 2, several adhesion bands over a wider area were found. Rather extensive and very ex-

TABLE III  
PLIABLE SOFT SURGICAL SILK (BRAND B, SIZE 2)

DOG NUMBER	DATE OPERATED	DATE AUTOPSIED	ADHESION GRADE*	REMARKS
SS-D56	9/12/38	10/11/38	Grade 3½	Adhesions gut, omentum, mesentery, points thick exudate about stitches
SS-D55	9/12/38	10/11/38	Grade 1	Only thin strand omentum to knot area; no adhesions elsewhere
SS-D54	9/12/38	10/ 4/38	Grade 1	Strand omentum to knot area; no adhesions elsewhere
SS-D53	9/11/38	9/27/38	Grade 2	Omentum to proximal third of suture line; points of exudate about stitches
SS-D52	9/11/38	10/ 4/38	Grade 1-	Flimsy adhesion from appendix to proximal and suture line
SS-D51	9/11/38	10/ 4/38	Grade 1	Thin strand gut to gut proximal and suture line; drop of pus on rolling line apart
SS-D50	9/11/38	10/11/38	Grade 2½	Mesentery to proximal two-thirds of suture line and omentum to knot area

\*Grade 1 or less, 4; Grade 2 or more, 3; Grade 3 or more, 1; total number observed, 7.

TABLE IV  
TREATED SURGICAL SILK (SIZES 1 AND 2, BRAND A)

DOG NUMBER	DATE OPERATED	DATE AUTOPSIED	ADHESION GRADE*	SIZE OF SILK	REMARKS
SS-D41	9/ 1/38	10/ 4/38	Grade 3	1	Adhesions gut, omentum, mesentery of suture site
SS-D42	9/ 5/38	10/ 4/38	Grade 2½	1	Adhesious mesentery, omentum
SS-D43	9/ 5/38	10/ 4/38	Grade 2¾	1	Gut to self, omentum, bladder; grains of thick exudate stitch areas
SS-D44	9/ 5/38	10/ 4/38	Grade 1½	1	Two inches from curve end, omental adhesions; exudate on dissecting suture line
SS-D35	8/25/38	9/26/38	Grade 2½	1	Omentum to about 70 per cent of suture line; grains exudate stitch area
SS-D46	9/ 9/38	10/ 4/38	Grade 2¾	1	Omentum to 75 per cent of suture line
SS-D47	9/ 9/38	10/11 /38	Grade 2	1	Omentum along suture line
SS-D49	9/ 9/38	10/ 9/38	Grade 1	2	Omentum to proximal end (not knot end)
SS-D48	9/ 9/38	10/11/38	Grade 1½	2	Omentum to knot area
SS-D45	9/ 5/38	10/ 4/38	Grade 2½	2	Gut to gut, omentum, mesentery
SS-D33	8/ 5/38	8/25/38	Grade 3½	2	More trauma than usual
SS-D32	8/ 5/38	8/25/38	Grade 1	2	Pus on rolling apart suture line
SS-D29	8/ 3/38	8/25/38	Grade 1+	2	Thick band to knot area; pus on rolling apart suture line
SS-D28	8/ 3/38	8/25/38	Grade 2½	2	Omentum to suture line
SS-D27	7/30/38	8/25/38	Grade 3	2	Omentum to suture line; adhesion mesentery; drops exudate suture line

\*Grade 1 or less, 2; Grade 2 or more, 10; Grade 3 or more, 3; Grade between 1 and 2, 1; Grade between 2 and 3, 6; total number observed, 15.



TABLE V

CATGUT 20-DAY CHROMIC 00 NONBOILABLE ON INTESTINAL NEEDLE

DOG NUMBER	DATE OPERATED	DATE AUTOPSIED	ADHESION GRADE*	REMARKS
SS-D36	8/28/38	9/16/38	Grade 2½	Omentum to 50 per cent of suture line; catgut present at autopsy
SS-D37	8/28/38	9/26/38	Grade 2½	Omentum to suture line and to mesentery
SS-D38	8/28/38	10/ 4/38	Grade 1½	Three-fourth inch attachment omentum to knot area; none elsewhere
SS-D39	8/28/38	10/ 4/38	Grade 1	Thin strand omentum to knot area
SS-D40	8/28/38	10/ 4/38	Grade 3	Loops, omentum, mesentery adhered at site

\*Grade 1 or less, 1; Grade 2 or more, 4; Grade 3 or more, 1; total number observed, 5.

tensive or massive adhesions were denoted by the Readings 3 to 4 respectively. Only adhesions occurring at or involving the experimental suture material site were considered. Adhesions at the abdominal incision area were not considered unless they involved the experimental gut area also, and this was practically never the case.

TABLE VI

CATGUT AND SILK SAME ANIMAL

DOG NUMBER	DATE OPERATED	DATE AUTOPSIED	ADHESION GRADE*	MATERIAL	SITE	REMARKS
S7-D14	12/ 1/37	12/29/37	Grade 1	Catgut	Cecal	
S7-D14	12/ 1/37	12/29/37	Grade 2	Silk	Proximal	
S7-D18	12/ 9/37	1/12/38	Grade 2	Catgut	Proximal	
S7-D18	12/ 9/37	1/12/38	0	Silk	Cecal	
S7-D19	12/20/37	1/ 5/38	Grade 1	Catgut	Proximal	At knot only
S7-D19	12/20/37	1/ 5/38	Grade 2	Silk	Cecal	At knot only
S7-D20	12/20/37	1/27/38	Grade 1	Silk	Cecal	
S7-D20	12/20/37	1/27/38	Grade 1	Catgut		

Catgut: Grade 2, 1; Grade 1, 3. Silk: Grade 2, 2; Grade 1, 1; Grade 0, 1.

## ANALYSIS OF RESULTS

Table VII presents in tabulated form some of the more important conclusions which we have reached from this study. As seen in Table VII, Grade 1 or less adhesions occurred with the department store silk in 68.4 per cent of 19 animals; whereas, this small degree of adhesion formation occurred in only 23.5 per cent of 17 animals in which chromic twenty-day nonboilable 0 suture on an intestinal needle was used for the experimental Noble plications of the small intestine. It is of interest to note that the Size 2 surgical silk of soft pliable nature and a brand in which we feel certain no wax or oil treatments are used, there were 57.1 per cent instances in which Grade 1 or less adhesions occurred as compared to 23.5 per cent in which chromic 0 was used and 20 per cent in which chromic 00 was used (the latter being essentially comparable in size to Size 2 silk); and 13.3 per cent when Sizes 1 and 2 specially treated silk were used (Table VII).

TABLE VII

PERCENTAGE AND DEGREE OF ADHESION FORMATION TO VARIOUS SUTURE MATERIALS

	GRADE 1 OR LESS	GRADE 2 OR MORE	GRADE 3 OR MORE	TOTAL NUMBER OF ANIMALS OBSERVED
Chromic 20-day nonboilable 0	23.5%	58.8%	17.6%	17
Department store silk	68.4%	15.7%	5.2%	19
Size 1				
Soft pliable surgical silk	57.1%	42.8%	14.2%	7
Brand B				
Size 2				
Treated surgical silk	13.3%	60.6%	20%	15
Brand A				
Sizes 1 and 2				
Chromic 20-day nonboilable 00	20%	80%	20%	5

In view of claims made for the brand of treated surgical silk used that "it has no chemical or allergic reaction and is non-irritating, eliminating the possibility of suppuration" it is interesting to note that in our series drops of pus or thick exudate formed rather consistently along the suture lines of this material. The softer "untreated" silks were far less consistently associated with gross exudate formation as well as with much less adhesion formation. It is true that the tensile strength of the special Brand A silk is greater size for size than the other silks used here. For example, the department store silk had, as measured by rough methods, a tensile strength of about two and one-half pounds; whereas, the tensile strength of the similar size special Brand A was listed as three pounds or over by the manufacturer. The markedly less tendency to cause adhesion formation, however, of the softer silks (including the Size 2 untreated surgical silk which we believe had as much tensile strength as the Size 1, Brand A treated silk) causes us to conclude that the treatment process used in preparation of the treated silk made this suture less satisfactory for general use inside the peritoneal cavity than if it had been untreated; and that needed tensile strength had best be obtained by using a slightly larger untreated silk than by using a silk hardened and treated as is Brand A, even though the latter be smaller in caliber per tensile strength unit. Certainly the wide claims made by the manufacturer regarding Brand A and its inertness in the tissues with the possibility of suppuration being eliminated seem unwarranted.

It might appear that a comparison between silk and catgut would not be warranted in instances when the catgut used was larger than the silk. The tensile strength of silk is, however, generally speaking, greater than that of catgut of the same size. No consistent accurate comparison between the tensile strength of catgut and silk is practical at the present time, since, with different brands of both materials, considerable variations in strength may exist; and variations also frequently exist from time to time in the same brands. Whipple evidently uses a Size C silk

TABLE V

CATGUT 20-DAY CHROMIC 00 NONBOILABLE ON INTESTINAL NEEDLE

DOG NUMBER	DATE OPERATED	DATE AUTOPSIED	ADHESION GRADE*	REMARKS
S8-D36	8/28/38	9/16/38	Grade 2 $\frac{1}{2}$	Omentum to 50 per cent of suture line; catgut present at autopsy
S8-D37	8/28/38	9/26/38	Grade 2 $\frac{1}{2}$	Omentum to suture line and to mesentery
S8-D38	8/28/38	10/ 4/38	Grade 1 $\frac{1}{2}$	Three-fourth inch attachment omentum to knot area; none elsewhere
S8-D39	8/28/38	10/ 4/38	Grade 1	Thin strand omentum to knot area
S8-D40	8/28/38	10/ 4/38	Grade 3	Loops, omentum, mesentery adhered at site

\*Grade 1 or less, 1; Grade 2 or more, 4; Grade 3 or more, 1; total number observed, 5.

tensive or massive adhesions were denoted by the Readings 3 to 4 respectively. Only adhesions occurring at or involving the experimental suture material site were considered. Adhesions at the abdominal incision area were not considered unless they involved the experimental gut area also, and this was practically never the case.

TABLE VI

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DOG NUMBER	DATE OPERATED	DATE AUTOPSIED	ADHESION GRADE*	MATERIAL	SITE	REMARKS
S7-D14	12/ 1/37	12/29/37	Grade 1	Catgut	Cecal	
S7-D14	12/ 1/37	12/29/37	Grade 2	Silk	Proximal	
S7-D18	12/ 9/37	1/12/38	Grade 2	Catgut	Proximal	
S7-D18	12/ 9/37	1/12/38	0	Silk	Cecal	
S7-D19	12/20/37	1/ 5/38	Grade 1	Catgut	Proximal	At knot only
S7-D19	12/20/37	1/ 5/38	Grade 2	Silk	Cecal	At knot only
S7-D20	12/20/37	1/27/38	Grade 1	Silk	Cecal	
S7-D20	12/20/37	1/27/38	Grade 1	Catgut		

Catgut: Grade 2, 1; Grade 1, 3. Silk: Grade 2, 2; Grade 1, 1; Grade 0, 1.

## ANALYSIS OF RESULTS

Table VII presents in tabulated form some of the more important conclusions which we have reached from this study. As seen in Table VII, Grade 1 or less adhesions occurred with the department store silk in 68.4 per cent of 19 animals; whereas, this small degree of adhesion formation occurred in only 23.5 per cent of 17 animals in which chromic twenty-day nonboilable 0 suture on an intestinal needle was used for the experimental Noble plications of the small intestine. It is of interest to note that the Size 2 surgical silk of soft pliable nature and a brand in which we feel certain no wax or oil treatments are used, there were 57.1 per cent instances in which Grade 1 or less adhesions occurred as compared to 23.5 per cent in which chromic 0 was used and 20 per cent in which chromic 00 was used (the latter being essentially comparable in size to Size 2 silk); and 13.3 per cent when Sizes 1 and 2 specially treated silk were used (Table VII).

## CONCLUSIONS

1. Comparative studies were made regarding the use of the following in the peritoneal cavities of dogs: department store silk of size essentially equivalent to Size 1 surgical silk; Sizes 1 and 2 specially treated waxed surgical silk of popular brand; chromic 0 and chromic 00 non-boilable twenty-day catgut on an intestinal needle (produced by a popular and reliable firm); and Size 2 soft, pliable, "untreated" surgical silk. Our experiments indicate that soft, pliable black silk (Size 1 or less) untreated by special waxing or other processes may be utilized as a continuous suture in long strands in the peritoneal cavity with little tendency for adhesions or other untoward complications to develop along the silk suture line from the suture material per se. Considerably less adhesion formation occurred about the department store silk and the soft pliable surgical silk than any of the other suture materials studied. The most extensive adhesion formation in this series occurred about a popular brand of surgical silk which is prepared by a special process including waxing. Pus and points of thick exudate were also found more frequently at autopsy about this latter material than any of the others.

Our observations would support those of other investigators that untreated silk becomes slowly absorbed in the tissues.

2. Wherever silk or catgut knots of any type are left exposed in the peritoneal cavity, permanent adhesions to the knot area will form in a very high percentage of instances.

3. We feel that occasionally clinical application of the Noble plication procedure is indicated.

We wish to thank Dr. Clock of the Davis-Geck Company for furnishing us with the catgut sutures used in these experiments; and Miss Daisy Thomson, operation room supervisor at the Little Rock General Hospital, for her cooperation.

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(two sizes smaller than Size 1) as comparable to a Size 0 catgut; and the latter is definitely larger in size than the former.<sup>9</sup> Therefore, although we have made some comparisons here of catgut and silk of similar sizes, such as the Size 2 silk as compared with 00 chromic catgut, we were nevertheless more interested in a comparison of the materials in sizes which are of approximately the same tensile strength.

In only five animals did we use chromic twenty-day Size 00 intestinal suture. The readings with this material were so consistently similar to those in the animals in which chromic 0 had been used, however, that we felt sufficient evidence had been accumulated to warrant conclusions that the percentage of adhesion formation will be consistently greater with Size 0 or Size 00 catgut than it will with a fine pliable soft silk of a tensile strength comparable to that of the catgut.

We did not incorporate in Table VII the readings in which catgut and silk were used in the same abdomen. We concluded relatively early that the manipulation attendant upon the use of the two materials in the same animal together with other considerations might allow for confusion of readings. Table VI, though included here, is therefore superfluous to our final conclusions.

The marked consistency with which a band of omentum permanently attached itself to exposed knots bears out the long recognized but frequently neglected fact that where knots are left exposed in the peritoneal cavity adhesions are almost sure to form. In our experiments these adhesions to the knot areas seemed as likely to occur about one suture material as the other.

In two animals of Table II we found that the silk strands tended eventually to migrate a certain distance leaving a free end. In one instance a free end one-half inch long had not become encapsulated or fixed thirty-six days after the original operation. In another animal a free silk end had become adherent to the adjacent mesentery and was simply encapsulated upon this structure thirty-five days after its original insertion. In neither case was there any sign of adhesions about these ends.

In one animal of Table II (department store silk) killed five months and three days after the original operation, there was evidence that some definite absorption of the silk suture had taken place. The strand could still be definitely identified and dissected out, but it was much more fragile and softer and could be much more easily pulled apart than it could have been originally. We would make a rough estimate that this strand would have almost, if not completely, disappeared in another six or eight months. Possibly 50 per cent of the dye in the black silk had been absorbed. The strand presented a dark, dirty, gray color.

experience seems to indicate furthermore that the etiology and pathogenesis are relatively unimportant factors in the surgical treatment and prognosis of this disease. Moreover, when the time has come for operation, the cyst has often grown to such proportions that the lining of the wall is destroyed and the origin can then only be guessed at. Lahey and Eckerson<sup>3</sup> have recently brought the classification of these cysts up to date, and it may be well to repeat it here: (1) Wolffian cysts, arising from any part of the early urogenital system; (2) lymphatic or chylous cysts, from developmental or obstructive phenomena of the retroperitoneal or mesenteric lymphatic system, lined merely by fibrous tissue or occasionally by endothelium; (3) Dermoid cysts, from imperfect closure of the abdominal plates, or from strayed genital cells or supernumerary ovaries; (4) mesocolic cysts, described by Handfield-Jones, from pockets of peritoneum left between the opposed serous surfaces of the mesentery and parietal peritoneum in the early rotation of the colon from the left to the right; (5) inflammatory cysts from broken down tuberculous glands, and parasitic cysts; and (6) traumatic blood cysts.

An accurate estimate of the frequency of this condition is not possible as the authors have not considered all of these cysts in the same category. In 1932 Warfield had found approximately 500 cases of mesenteric cysts; whereas, Wyatt<sup>7</sup> in 1931 had collected 46 cases of omental cysts. Peterson<sup>8</sup> stated that the usual ratio of mesenteric to omental cysts is 5 to 1, but from the above figures it would seem that the ratio is more nearly 10 to 1. Of our 18 cases, 3 were omental cysts, 5 were mesenteric cysts, and 10 were cysts which arose from behind the posterior peritoneum. No case in which the cyst was traceable to an adult, fully formed organ, such as intestine, kidney, ovary, or pancreas, has been included in this report.

Although retroperitoneal cysts may occur at any age, as noted in Table I, it is seen that many of the patients were young. Even in the older group, one gets the impression that the condition had existed for many years but had gone unrecognized while the patient was young. These facts point strongly to the congenital origin of these cysts. Interestingly enough, retroperitoneal cysts, unlike most congenital anomalies, are not accompanied by any other congenital deformity. Furthermore, the family histories of our patients failed to reveal that any other member of the family had suffered from a retroperitoneal cyst. These facts would indicate that this type of cyst represents an accidental malformation in the development of some primitive embryonic structure. A survey of the past histories of these patients gave no clue as to the cause of cyst formation. Only two of the eighteen patients had been subjected to previous abdominal operation, and in neither case was it evident at operation that the previous laparotomy had anything to do with subsequent formation of a cyst. No history of severe abdominal

# CYSTS OF THE OMENTUM, MESENTERY, AND RETROPERITONEUM

## A CLINICAL STUDY OF EIGHTEEN CASES

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CYSTS of the omentum, mesentery, and retroperitoneum have been reported in the literature on frequent occasions during the past few decades. Many of the communications have dealt with isolated cases and have given detailed descriptions of the complications which arose during their course. Because the main interest in this subject has centered around the origin and rarity of these cysts, most of the reports have concentrated upon discussions of classification and etiology.

Within the past twenty three years, 18 patients with cysts of the omentum, mesentery, and retroperitoneum have been operated upon at the Jewish Hospital of Brooklyn. Inasmuch as an individual surgeon will encounter but a few cases in an entire career, it was thought profitable to review and analyze all of the cases of this kind in an attempt to gain a broader knowledge of the subject. It is our purpose to report the clinical picture in detail and to outline the surgical treatment and results obtained.

Handfield-Jones<sup>1</sup> gave as his definition of a retroperitoneal cyst: "Those cysts which have no apparent connections with any adult anatomical structure except areolar tissue." Pemberton and Mahorner<sup>2</sup> also stressed the point that a true retroperitoneal cyst must arise in areolar tissue and cannot spring from any fully formed organ. Lahey and Eckerson<sup>3</sup> state that mesenteric, omental, and retroperitoneal cysts must actually be grouped in the same category, since the mesenteric and omental variety are merely anterior extensions, or inclusions, of those which were originally retroperitoneal. We are in agreement with these authors in their views that pathologically and embryologically these cysts can all be classed as retroperitoneal, and in this paper we have more or less considered them as one lesion. However, to denote more accurately their location, we have continued to refer to them as omental, mesenteric, and retroperitoneal.

Much has been written on the classification and origin of these various cysts and it is hardly advantageous to repeat the theories in a clinical study of this kind. For detailed information concerning theories of origin, the reader is referred to the excellent contributions of Dowd,<sup>4</sup> Handfield-Jones,<sup>1</sup> Stoney,<sup>5</sup> Lahey and Eckerson,<sup>3</sup> and Warfield.<sup>6</sup> Our

Pain appeared to be more or less constant, did not radiate, and bore no relation to food intake. Although the pain was rather intense in most cases, it was not colicky nor so excruciating as to require sedation. Two of the 3 patients with omental cysts suffered abdominal pain; 4 of the 5 with mesenteric cysts had abdominal pain; whereas only 4 of the 10 with cysts located in the retroperitoneal space suffered from this symptom. The absence of pain in such a large percentage of those patients with cysts arising from beneath the posterior peritoneum can be explained by the fact that the retroperitoneal space is elastic and permits the growth of an extensive tumor without the production of pressure symptoms.

Nausea, vomiting, and anorexia were not very prominent symptoms except in those patients who were admitted in an acutely ill state. Six patients, 5 of them acutely ill, told of nausea or vomiting and all suffered from a cyst either in the omentum or mesentery. The absence of nausea and vomiting in the cases of retroperitoneal cyst is characteristic of a lesion which produces practically no peritoneal irritation because of its extraperitoneal location. Although Moynihan described rapid emaciation as an outstanding symptom of chylous cysts, marked loss of weight was noted in but 2 of the 18 patients and oddly enough neither of these patients had cysts which contained chylous fluid. Bowel function did not appear to be greatly disturbed as 14 patients told of normal bowel movements, diarrhea occurred in 2 patients, constipation in 1 patient, and obstipation in another. The 2 patients with diarrhea had tarry stools, the origin being hemorrhage from a duodenal ulcer in the one and of undetermined origin in the other. The patient with obstipation was the only case in this series who had symptoms of intestinal obstruction. Temperature on hospital admission was normal in all but 6 cases. These 6 patients were acutely ill, but the temperature ranged only from 100° F. to 101° F.

A palpable mass was found in 11 of the 18 patients. It is surprising that, although the omentum is one of the most superficial intraperitoneal structures, none of the patients with an omental cyst presented a palpable tumor. Four of the 5 patients with mesenteric cysts presented a tumor. A striking feature of these mesenteric cysts was their extreme mobility. In 2 cases we were able to move the mass upward to the level of the epigastric angle and downward to the level of the pubic crest. Seven of the 10 patients with retroperitoneal cysts were found to have a mass on abdominal or rectovaginal examination. In this group the tumors were always noted to be in the same location and were immobile and fixed.

Abdominal tenderness was found on physical examination in 11 patients. There did not seem to be any correlation between the presence of a palpable mass and the existence of abdominal tenderness, for 5 patients with a palpable tumor experienced no abdominal tenderness;



trauma was elicited in any patient, nor was there any patient who had known of a parasitic or tuberculous infection. Five of our patients were less than 10 years of age; whereas, ten patients were under 30 years old. It is also noted (Table I) that the condition was more common in females, there being 11 female and 7 male patients.

TABLE I

AGE	MALE	FEMALE	OMENTAL CYSTS	MESENTERIC CYSTS	RETRO- PERITONEAL CYSTS	TOTAL
1-10 yr	2	3	2	2	1	5
10-20 yr.	1	1	0	1	1	2
20-30 yr	2	1	0	1	2	3
30-40 yr.	0	3	0	0	3	3
40-50 yr.	1	2	0	1	2	3
50-60 yr.	1	1	1	0	1	2
Total	7	11	3	5	10	18

Moynihan<sup>9</sup> divided symptoms and signs of retroperitoneal cysts into three varieties: first, those with no symptoms whatever; second, those who followed a chronic course with the patient complaining of an abdominal tumor and occasional attacks of slight pain and indigestion; and third, those with acute symptoms. A review of the cases in this series leads us to divide symptoms and signs into two main groups of patients; a first group composed of those in whom acute symptoms including abdominal pain are the outstanding features, and a second group comprised of those in whom the presence of a tumor mass constitutes almost the entire picture of the condition.

In our series 8 cases were admitted to the hospital as acute surgical conditions. Six of these cases were suffering from their initial attack, while 2 patients had had symptoms on and off for several months prior to hospital admission. The other 10 patients had been more or less chronically ill for a period of time varying from a few months to a few years. Eight of these chronically ill patients were admitted to the hospital because an abdominal mass had been palpated by the family physician; the ninth sought admission because of progressive swelling of the abdomen, and the tenth patient was sent into the hospital for operation for a duodenal ulcer.

Twelve of the 18 patients, including all of the acute cases and 4 of the chronic cases, had at one time or another suffered from abdominal pain. As one might expect, the pain was much more severe in those patients who were acutely ill. One of the main characteristics of the pain was its failure to localize, as evidenced by the fact that in 10 of the 12 patients the pain was described as being "all over the abdomen." The other 2 patients localized the pain to the region directly over the tumor mass. Since the pain in retroperitoneal cysts is in many instances caused by stretching of the overlying peritoneal surface, one can understand its widespread distribution and its failure to localize to any one area.

hospital will not be accurately diagnosed. The 18 patients in this series were attended by 7 different surgeons and no surgeon handled more than 5 cases. Furthermore, 8 of the patients entered the hospital with acute symptoms of such intensity that any characteristic signs of an omental, mesenteric, or retroperitoneal cyst were almost completely hidden. Of these, 5 patients were thought to have acute appendicitis and the other 3 acutely sick patients were diagnosed as having intestinal obstruction, acute diverticulitis, and an abdominal tumor of unknown origin. Although an accurate, correct diagnosis was not made in any instance, 7 of the 10 patients who had been chronically ill and who presented few or no acute symptoms were thought to have an abdominal cystic tumor. Of these, ovarian cyst was named as the underlying lesion in 4 cases, omental cyst was suspected in 2 cases, 1 of which proved to be a mesenteric cyst and the other, a retroperitoneal cyst; and solitary cyst of the kidney was the diagnosis in the seventh patient. The 3 remaining patients were thought to have hepatic cirrhosis, duodenal ulcer, and an abdominal tumor of undetermined etiology.

TABLE II

SYMPTOMS AND SIGNS	OMENTAL CYSTS 3 CASES (PERCENTAGE)	MESENTERIC CYSTS 5 CASES (PERCENTAGE)	RETROPERI- TONEAL CYSTS 10 CASES (PERCENTAGE)	TOTAL 18 CASES (PERCENTAGE)
Abdominal pain	66.6	80.0	60.0	66.6
Palpable tumor mass	0.0	80.0	70.0	61.1
Abdominal tenderness	66.6	80.0	50.0	61.1
Nausea and vomiting	100.0	60.0	0.0	33.3
Marked weight loss	33.3	0.0	10.0	11.1
Constipation	0.0	20.0	10.0	11.1
Diarrhea	33.3	0.0	10.0	11.1
Abdominal muscle rigidity	66.6	40.0	10.0	27.7
Ascites	33.3	0.0	0.0	5.5
Dull or flat percussion note over mass	66.6	40.0	30.0	38.8
Albuminuria	33.3	40.0	60.0	50.0

In a rather young patient with a smooth, circumscribed abdominal tumor, generalized pain located all over the abdomen and moderate abdominal tenderness, one should consider the possibility of a retroperitoneal cyst. Also, the absence of signs of emaciation and anemia so often seen with malignant tumors of the abdominal region and the presence of albuminuria should be helpful in leading one toward a diagnosis. However, much more often the condition will be suspected after excluding the gastrointestinal and urinary tracts as the cause of the symptomatology. Lahey and Eckerson, Hafezi, and others have stressed the great importance of x-ray examination of these organs as a means of reaching the diagnosis of omental, mesenteric, or retroperitoneal cyst. It is safe to state that the correct diagnosis would have been made more often in our series of cases had the surgeons resorted more frequently to x-ray investigations. The important issue is, nevertheless, that all

whereas, 5 patients with pain on abdominal palpation presented no discernible tumor. The cause for the abdominal tenderness was thought to be, in view of subsequent operative findings, hemorrhage into the cyst in 5 patients, rupture of the cyst wall with fluid in the peritoneal cavity in 3 patients, partial intestinal obstruction in 1 patient, and an accompanying mild catarrhal appendicitis in 1 patient. The cause of tenderness was not apparent in the eleventh patient who exhibited this symptom.

Abdominal muscle rigidity was found in only 5 patients, and in all of these either hemorrhage into the cyst or rupture of the cyst wall had occurred preoperatively.

A diagnosis of ascites was made in 1 patient because of a fluid wave and on operation this patient was found to have a huge omental cyst occupying almost the entire abdominal cavity. Schwartzenger,<sup>10</sup> Wyatt, and Halsted<sup>11</sup> have also reported cases of omental cysts which had been tapped for ascites. This finding can be explained by the fact that cysts of the omentum often grow to huge dimensions and, being thin walled, they tend to rupture easily.

A dull or flat percussion note was elicited over the region of the cysts in 7 cases. Although Hafezi<sup>12</sup> mentioned a dull percussion note over the cyst with an area of resonance around it as a characteristic sign of a retroperitoneal cyst, we would expect to obtain similar findings with any encapsulated solid tumor of the midabdominal region.

There were no characteristic blood count pictures in this series of cases although the more acutely ill the patient, the higher was the total white blood cell count and the greater was the percentage of polymorphonuclear leucocytes. All blood counts were normal in the chronic cases.

Albumin in the urine was found in 9 of 17 patients who had had a urine examination performed prior to operation. In reviewing the literature we were unable to discover any similar finding. It may be significant that 7 of these 9 patients with albuminuria had been chronically ill and had had symptoms for many months prior to hospital admission. A possible explanation may be that this function was somewhat disturbed by pressure of these cysts on the kidney or ureter. However, none of these patients exhibited other manifestations of urinary dysfunction and in 4 instances the cysts by their anatomic location could not have produced pressure on the ureters or kidneys.

Table II shows the incidence of the significant symptoms and signs in this series of cases.

The diagnosis of omental, mesenteric, and retroperitoneal cysts is attended with difficulty mainly because of the infrequent occurrence of the condition and because superimposed acute symptoms mask the picture. It is readily understood that a disease which is seen but 18 times in twenty-three years by numerous surgeons in a large metropolitan

hospital will not be accurately diagnosed. The 18 patients in this series were attended by 7 different surgeons and no surgeon handled more than 5 cases. Furthermore, 8 of the patients entered the hospital with acute symptoms of such intensity that any characteristic signs of an omental, mesenteric, or retroperitoneal cyst were almost completely hidden. Of these, 5 patients were thought to have acute appendicitis and the other 3 acutely sick patients were diagnosed as having intestinal obstruction, acute diverticulitis, and an abdominal tumor of unknown origin. Although an accurate, correct diagnosis was not made in any instance, 7 of the 10 patients who had been chronically ill and who presented few or no acute symptoms were thought to have an abdominal cystic tumor. Of these, ovarian cyst was named as the underlying lesion in 4 cases, omental cyst was suspected in 2 cases, 1 of which proved to be a mesenteric cyst and the other, a retroperitoneal cyst; and solitary cyst of the kidney was the diagnosis in the seventh patient. The 3 remaining patients were thought to have hepatic cirrhosis, duodenal ulcer, and an abdominal tumor of undetermined etiology.

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Albumin in the urine was found in 9 of 17 patients who had had a urine examination performed prior to operation. In reviewing the literature we were unable to discover any similar finding. It may be significant that 7 of these 9 patients with albuminuria had been chronically ill and had had symptoms for many months prior to hospital admission. A possible explanation may be that this function was somewhat disturbed by pressure of these cysts on the kidney or ureter. However, none of these patients exhibited other manifestations of urinary dysfunction and in 4 instances the cysts by their anatomic location could not have produced pressure on the ureters or kidneys.

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and the other two in the region of the cecum and ascending colon. One of these cysts was said to be about  $1\frac{1}{2}$  inches in diameter and the others were described as being the size of an orange or grapefruit. The 3 cysts which originated in the mesentery of the small bowel were a canary yellow color and contained milky, chylous fluid; whereas the 2 which arose from beneath the large bowel were bluish in color and contained serosanguineous fluid. None of the mesenteric cysts had ruptured pre-operatively; all but 1 were rather thick walled, and 4 of the 5 were uniloculated. There were 3 specimens obtained by resection and 2 of these showed merely a cyst wall made up of loose, fibrous tissue and no endothelium. The third cyst contained a flat endothelial lining surrounded by loose fibrous tissue structure.

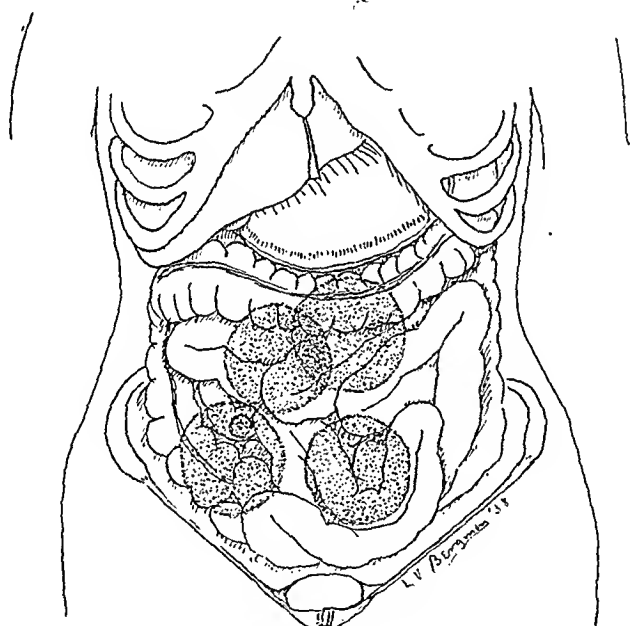


Fig. 2.—Sketch shows the approximate size and location of the five mesenteric cysts.

The remaining 10 cysts arose from behind the posterior parietal peritoneum. It is impossible to give an accurate description of their size since many were so extensive or deep seated that they could not be completely visualized at operation. However, the smallest of these cysts was described as being the size of a grapefruit and some were so large that the operating surgeons stated that they occupied almost an entire quadrant or one-half of the abdomen. Notes on the operative charts of 6 cases described the cysts as multiloculated; 2 were said to be uniloculated, and no statement concerning this point was made on the records of the other 2 cases. Four of the retroperitoneal cysts were located in the left lower quadrant of the abdomen either in the left iliac fossa or from the area mesial to the sigmoid or descending colon. Three

patients with an undiagnosed abdominal tumor or with symptoms denoting an abdominal surgical lesion should be subjected to exploratory laparotomy. If this procedure is carried out in doubtful cases, then the precise preoperative diagnosis assumes a role of minor importance.

Cysts of the omentum, mesentery, and retroperitoneum show little tendency to recur or to undergo malignant degeneration. Warfield found but 1 instance of malignant degeneration in a collected series of 129 mesenteric cysts. The gross appearance of these cysts is varied depending upon the nature of the contents and the thickness of the walls. The microscopic structure often affords little information, for pressure within the cyst frequently destroys the lining membrane. So far as operative recovery and prognosis are concerned, the gross and microscopic findings appear to be relatively unimportant factors.

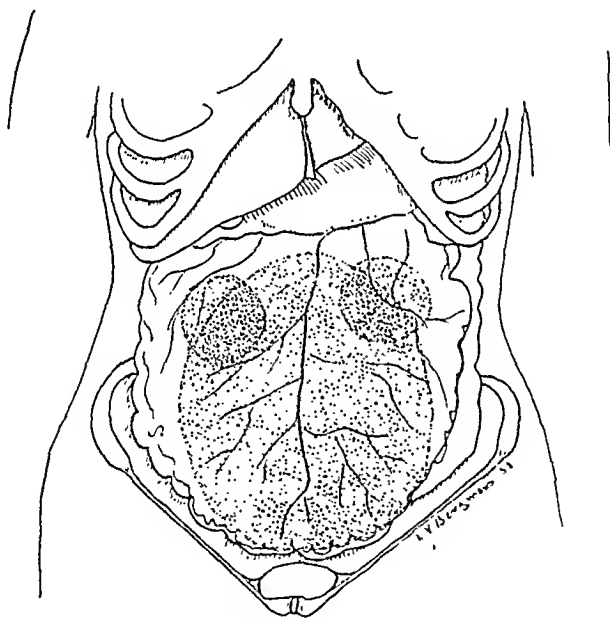


Fig. 1.—Sketch shows approximate size and location of the three omental cysts.

The three omental cysts were large, thin walled, and multiloculated. All had ruptured preoperatively as evidenced by the presence of sero-sanguineous fluid in the peritoneal cavity as well as within the cyst. On microscopic examination, two were found to be simple serous cysts with a flat, single layered endothelial lining surrounded by a thin fibrous tissue layer. The third cyst showed questionable signs of malignant degeneration, although no definite diagnosis was proffered. The changes were stated by the pathologist to be suggestive of an angioendothelioma.

There were five mesenteric cysts, two of which were located in the mesentery of the jejunum, one in the mesentery of the terminal ileum.

size. Furthermore, the thinness of the wall and the lack of a surgical capsule, particularly in those cysts located behind the posterior peritoneum, frequently makes complete enucleation impossible. Despite the fact that their attachments are largely areolar tissue, many of them, particularly those originating from behind the posterior peritoneum, extend so deeply that attempted resection is hazardous. Inasmuch as almost any one of the standard operations results in a cure, it is usually wisest to do that procedure which entails the least risk. Total removal was found practical in but 8 of our 18 cases; whereas, partial resection was carried out in 3 cases and marsupialization in 4 cases. The 3 remaining cysts were treated by simple incision and drainage.

TABLE III

SALIENT FEATURES OF CYSTS	OMENTAL CYSTS (3 CASES)	MESENTERIC CYSTS (5 CASES)	RETROPERI- TONEAL CYSTS (10 CASES)	TOTAL (18 CASES)
Number of multilocular cysts	3	1	6	10
Number of unilocular cysts	0	4	2	6
Cysts containing serous- guineous fluid	3	2	4	9
Cysts containing chylous fluid	0	3	2	5
Cysts containing straw- colored fluid	0	0	4	4
Cysts lined by endothelium or epithelium	3	1	4	8
Cysts lined only by fibrous tissue layer	0	2	3	5
Thin-walled cysts	3	1	?	4?
Thick-walled cysts	0	4	?	4?
Cysts which ruptured pre- operatively	3	0	1	4
Cysts showing malignant degeneration	1?	0	0	1?
Cysts measuring at least "size of grapefruit"	3	4	10	17
Cysts causing intestinal obstruction	0	1	0	1

Two of the 3 omental cysts were completely excised and the third, a cyst involving almost the entire greater omentum, was marsupialized. Three of the mesenteric cysts were resected, 1 was partially resected, and another was incised and drained. Three of the retroperitoneal cysts lent themselves to complete removal; 2 were partially removed; 3 were marsupialized; and 2 others were incised and drained (Table IV).

All patients made a satisfactory postoperative recovery, regardless of which particular procedure had been performed. There were 2 postoperative complications, but neither was severe enough to cause great alarm. One patient, on whom marsupialization had been done for a retroperitoneal cyst, developed an abscess within the cyst cavity necessitating incision and drainage. Another patient, on whom incision and drainage had been performed for a mesenteric cyst, made an uneventful



cysts were located in the right lower quadrant of the abdomen either from the area mesial to the cecum or from the right ileac fossa. One cyst was a multilocular chylous cyst arising from the lesser omental sac; another arose in the region of the transverse colon, and still another appeared to occupy almost the entire retroperitoneal space. Four of the 10 cysts appeared blue in color and contained serosanguineous or bloody fluid; 2 had a yellowish tinge and contained milky chylous fluid; and the other 4 cysts bore the color of the overlying peritoneum and were filled with straw-colored fluid. The majority of these cysts were thin walled, 1 having ruptured preoperatively and 2 having been accidentally ruptured during operative manipulations. A specimen for microscopic examination was obtained in 7 of these 10 cases. Two sections were

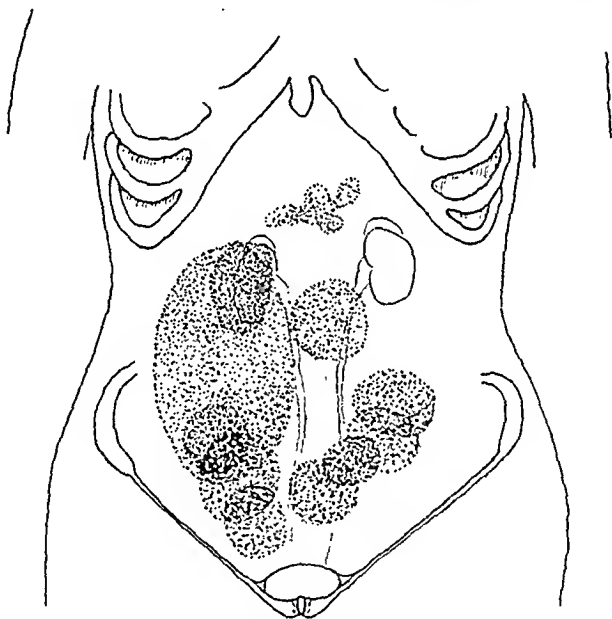


Fig. 3.—Sketch shows approximate size and location of the ten retroperitoneal cysts.

made up of a flat endothelial layer surrounded by a fibrous tissue structure and 1 specimen was composed of high columnar epithelium surrounded by loose fibrous tissue. The microscopic structure in 1 case resembled a papillary cystadenoma suggesting that the cyst might have originated from supernumerary or aberrant ovarian tissue. The 3 remaining specimens showed only a fibrous tissue layer with no endothelium or epithelium.

It is important to repeat that no tissue resembling intestinal, nephric, or pancreatic parenchyma was found on microscopic examination in any case. Table III outlines the salient features of the cysts.

Complete excision of the cysts is the preferred procedure, but this is often impractical because of their inaccessible location or their extensive

plicated cases of omental, mesenteric, and retroperitoneal cyst which have not been recorded in the literature because they lack interesting or unusual features.

Although there is incomplete information on the follow-up of these eighteen cases, it would appear that any one of the various operative procedures is adequate to produce a cure. Of the seven patients who were seen two to four years after operation, no recurrence of symptoms or signs of an abdominal tumor had taken place.

#### SUMMARY

1. An analysis of 18 cases of cysts of the omentum, mesentery, and retroperitoneum operated upon from 1915 to 1938 is presented.

2. Only those cysts which have no connections with any adult anatomic structure are included in this report. It is emphasized that omental, mesenteric, and retroperitoneal cysts all should be grouped as one, namely retroperitoneal, for embryologically and pathologically they have a similar origin.

3. In this series there were 3 omental, 5 mesenteric, and 10 cysts arising from behind the posterior peritoneum; 7 patients were males and 11 were females. Although these cysts occur at any age, 10 of the 18 patients were under 30 years of age.

4. Symptoms and signs can be divided into acute and chronic. The acute symptoms are often occasioned by hemorrhage into the cyst or rupture of the cyst wall. The chronic symptoms are usually mild, the main complaint being that of a progressively growing abdominal tumor. Principal symptoms and signs were (1) generalized, nonlocalizing, constant, abdominal pain; (2) palpable tumor mass; (3) abdominal tenderness. Albuminuria was noted in 9 cases.

5. The exclusion, by x-ray examination, of the gastrointestinal and urinary tracts as the seat of the pathology is helpful in establishing the diagnosis of omental, mesenteric, or retroperitoneal cyst.

6. Omental cysts are usually large, thin walled, multiloculated, and contain serosanguineous fluid. They tend to rupture easily, thus causing acute symptoms. Mesenteric cysts are often the size of a grapefruit, are thick walled, do not rupture easily but tend to cause intestinal obstruction. If they arise from the mesentery of the small bowel, they usually contain chylous fluid. Cysts arising from behind the posterior peritoneum grow to huge dimensions, are thin walled, occasionally rupture, and most often contain straw-colored or serosanguineous fluid.

7. Little information concerning the origin of these cysts can be gained through microscopic examination. The commonest findings are either a cyst wall composed of loose fibrous tissue structure alone or a flat endothelial layer surrounded by a fibrous tissue layer.

TABLE IV

OPERATIVE PROCEDURES	OMENTAL CYSTS (3 CASES)	MESENTERIC CYSTS (5 CASES)	RETROPERI- TONEAL CYSTS (10 CASES)	TOTAL (18 CASES)
Total excision	2	3	3	8
Partial excision	0	1	2	3
Marsupialization	1	0	3	4
Simple incision and drain- age	0	1	2	3

hospital recovery but three months later developed partial intestinal obstruction because of adhesions. Those patients on whom marsupialization or simple incision and drainage had been carried out, drained serous or serosanguineous fluid for a period varying from two weeks to two months. The average length of time of drainage from these wounds was approximately four weeks. The most satisfactory results were noted in those patients upon whom complete resection of the cysts had been performed. Primary wound healing and complete absence of symptoms were found in every one of these 8 cases.

The benign preoperative and postoperative course which almost all of the 18 patients in this series followed is in rather striking contrast to the findings of some other authors. At no time were any of our patients dangerously ill nor did we find the high incidence of surgical shock, massive hemorrhage, or intestinal obstruction which Warfield, Hafezi, and Peterson have reported. No patient in this series suffered from postoperative shock nor did hemorrhage follow cyst enucleation. Intestinal obstruction was found on hospital admission in but one case and peritonitis was never encountered. It is also noteworthy that none of the cysts were so located that they involved vital structures, such as intestine, bowel, pancreas, spleen, liver, kidney, or ureter. By its very definition, a true retroperitoneal cyst is one containing no attachments other than areolar tissue. One would expect, therefore, that even though there are intimate adhesions to adjacent organs lines of cleavage could be found which would obviate the necessity of resecting these neighboring structures. There are, of course, many exceptions in which important viscera, particularly bowel, are involved by proximity to the cyst and many such cases have been reported by Jewesbury,<sup>13</sup> Salazar, Panisello, and Pino,<sup>14</sup> Cornioley,<sup>15</sup> Muir,<sup>16</sup> Vezina,<sup>17</sup> Pagliani,<sup>18</sup> von Achmatowicz,<sup>19</sup> and others.

It is questionable whether the excellent results obtained in this series of cases can be attributed to any superior technique or therapeutic measure. The more logical assumption is that the literature gives a somewhat false picture of the severity of this condition inasmuch as so many of the reports deal with unusual and complicated cases. It seems fair to assume that there are a much greater number of simple, uncom-

## PHYSIOLOGIC INDICATIONS IN PEPTIC ULCER DIETS\*

ALBERT F. R. ANDRESEN, M.D., BROOKLYN, N. Y.

IT IS indeed a great pleasure and satisfaction to me to have been invited to address a meeting of surgeons on the subject of ulcer diets. Having seen repeatedly the prompt relief of ulcer symptoms by some diet bearing someone's name (like Lennhartz, Lenbe, Sippy, Smithies, and others), an observer is apt to feel that there is some occult reason for this, that the ulcer is being "cured" by the diet. If, however, in addition to the diet, some medication has been used, whether by the oral or parenteral route, credit seems to be taken away from the diet and given to the other treatment. Yet we know from careful history taking that attacks of ulcer symptoms are usually self-limited, and Cole and other roentgenologists have demonstrated that without treatment, and at times probably in spite of treatment, ulcers become smaller and disappear entirely within a comparatively short time. This accounts for the surgical experience of finding no ulcer when patients have procrastinated too long after their x-rays before consenting to operation, and for the frequent finding at autopsies of often multiple scars of healed ulcers in patients who died of other conditions. We are certainly justified in accepting the dictum that a peptic ulcer is an acute process, healing rapidly and spontaneously, and that each attack of symptoms is due to a new ulcer. This conception simplifies the approach to the ulcer problem and makes us realize that the only ulcers which do not heal and in which therefore the symptoms do not disappear are the ones with complications. And it is in these complicated ulcers that surgical intervention is so frequently required. If the average medical practitioner would learn to recognize the complicated ulcers and realize that they are difficult problems, requiring careful study and a definite program of therapy, the many misunderstandings between internist and surgeon would cease to exist.

### INDICATIONS FOR TREATMENT

In general, the indications for treatment in uncomplicated peptic ulcer may be summed up as follows: First, giving the ulcer an opportunity to heal spontaneously, which can best be accomplished by more or less complete rest and proper diet; second, treating any complications which may develop, including operation for perforation and obstruction and rest and diet for hemorrhage; third, pre-

\*Read at a symposium of the American College of Surgeons at the Methodist Episcopal Hospital, Brooklyn, N. Y., October 19, 1938.  
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8. All 18 patients recovered following operation. Wherever possible, complete resection should be performed, but, if complete enucleation makes a hazardous procedure of the operation, then marsupialization or simple incision and drainage of the cyst is sufficient. These cysts show little tendency to recur or to undergo malignant degeneration. We did not find it necessary to do extensive surgery, for complications such as others have reported in the literature did not occur in our series of cases.

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been using for the past twenty years or more to conform to all of the above requirements is as follows:

*Breakfast:*

Milk, 1 glass  
Cereal, full dish, with cream and sugar  
Egg, soft boiled or poached  
Bread or toast and butter  
Fruit juice (at end)

*Midmorning:*

Milk, 1 glass (with added cream and glucose, if desired)  
Crackers, bread, cake, or jello

*Luncheon:*

Milk, 1 glass  
Egg, soft boiled or poached, or cream cheese  
Potato, baked or mashed, or plain spaghetti  
Vegetables, strained or mashed  
Bread and butter  
Pudding, jello, ice cream, or stewed fruit

*Midafternoon:*

Same as for midmorning

*Supper:*

Same as for breakfast or luncheon

*At bedtime* (and during night every 2½ hours if awake):

Same as for midmorning

With the above diet we permit the use of salt, but no other condiments. The drinking of at least six glasses of water per day is insisted upon. Olive oil, one-half ounce three times daily, before feedings is usually prescribed and mineral oil, ½ ounce at bedtime, is necessary. Although the diet itself contains sufficient vitamins, they may be added to by the administration of single or combined vitamin preparations. Iron, calcium, and phosphorus may also be added as indicated.

The effect of this diet should be an immediate relief of symptoms. Within twenty-four or forty-eight hours the patient should be comfortable and free of pain, whether ambulatory or at rest. Failure to get relief indicates one of three things, as follows:

1. *An Incorrect Diagnosis.*—Frequently patients are prescribed an ulcer diet on suspicion that their symptoms may be caused by ulcer, and usually the symptoms are relieved by the diet, because it is beneficial in many gastrointestinal conditions. But occasionally some other condition, like partial intestinal obstruction, renal irritation, or cardiac pain, may be the cause of the symptoms and no relief will be experienced. The solution of this difficulty consists in making a correct diagnosis before instituting treatment.

2. *Allergy*, even though an ulcer has been shown to be present, may produce persistent symptoms, as mentioned previously, and should be suspected where the patient's history shows previous allergic mani-

venting, if possible, the occurrence of more ulcers in the future by thorough removal of all focal infections and by the avoidance of allergic irritation. In discussing physiologic indications for the treatment of ulcer, it is well to realize how the normal physiology of the stomach is disturbed by the presence of the ulcer. An uncomplicated ulcer causes an increased irritability of the stomach, producing exaggerated peristaltic and hunger contractions, and especially, if near the pylorus, spasm in this region. These conditions produce the pains of ulcers. If the ulcer is in the duodenum or if it is complicated by other conditions beyond the pylorus (cholecystitis, appendicitis, colitis), retrostaltic waves may be initiated which manifest themselves by uneasy or full feelings in the upper abdomen, the desire to belch, and the occurrence of heartburn, sour eructations, or vomiting. If the patient is suffering from food allergy, the ingestion of foods to which the stomach is sensitized will aggravate all symptoms and may produce marked hyperemia and edema with obstructive symptoms or hemorrhages or may simply cause persistent pain. If the patient has been afraid to eat, the diet may have been reduced to subnormal requirements, resulting not only in loss of weight but also in the development of definite symptoms of food deficiency. If the patient has been taking alkalis to excess, he may be suffering from an alkalosis, and either alkalosis or acidosis together with hypochloremia may occur as a result of vomiting.

The physiologic disturbances just mentioned all can be alleviated by a proper diet.

#### DIETETIC INDICATIONS

Pain, whether due to hunger contractions or spasm, can be relieved by frequent feedings, which substitute the more quiet and deliberate peristaltic contractions for the excessive, painful hunger contractions. Irritation, in general, can be relieved by bland, soothing foods except where such foods are known to cause allergic manifestations, in which case those particular foods must be avoided. For milk, the most frequent offender, it is often difficult to find a substitute, but I have found that a 3 to 5 per cent flavored gelatin solution in water makes a very acceptable and nutritious drink. Retrostaltic symptoms are avoided by giving food in sufficient quantities to stimulate forward peristaltic waves of adequate strength to overcome the reverse waves, and by giving it frequently. Symptoms of food deficiency must be avoided or, if present, caused to disappear by properly balanced rations, paying particular attention to protein, vitamins, and minerals. Alkalosis, acidosis, or hypochloremia may require temporarily the parenteral administration of glucose and saline solutions, but usually the diet should take care of these conditions. The diet which I have

been using for the past twenty years or more to conform to all of the above requirements is as follows:

*Breakfast:*

Milk, 1 glass  
Cereal, full dish, with cream and sugar  
Egg, soft boiled or poached  
Bread or toast and butter  
Fruit juice (at end)

*Midmorning:*

Milk, 1 glass (with added cream and glucose, if desired)  
Crackers, bread, cake, or jello

*Luncheon:*

Milk, 1 glass  
Egg, soft boiled or poached, or cream cheese  
Potato, baked or mashed, or plain spaghetti  
Vegetables, strained or mashed  
Bread and butter  
Pudding, jello, ice cream, or stewed fruit

*Midafternoon:*

Same as for midmorning

*Supper:*

Same as for breakfast or luncheon

*At bedtime* (and during night every 2½ hours if awake):

Same as for midmorning

With the above diet we permit the use of salt, but no other condiments. The drinking of at least six glasses of water per day is insisted upon. Olive oil, one-half ounce three times daily, before feedings is usually prescribed and mineral oil, ½ ounce at bedtime, is necessary. Although the diet itself contains sufficient vitamins, they may be added to by the administration of single or combined vitamin preparations. Iron, calcium, and phosphorus may also be added as indicated.

The effect of this diet should be an immediate relief of symptoms. Within twenty-four or forty-eight hours the patient should be comfortable and free of pain, whether ambulatory or at rest. Failure to get relief indicates one of three things, as follows:

1. *An Incorrect Diagnosis.*—Frequently patients are prescribed an ulcer diet on suspicion that their symptoms may be caused by ulcer, and usually the symptoms are relieved by the diet, because it is beneficial in many gastrointestinal conditions. But occasionally some other condition, like partial intestinal obstruction, renal irritation, or cardiac pain, may be the cause of the symptoms and no relief will be experienced. The solution of this difficulty consists in making a correct diagnosis before instituting treatment.

2. *Allergy*, even though an ulcer has been shown to be present, may produce persistent symptoms, as mentioned previously, and should be suspected where the patient's history shows previous allergic mani-



festations elsewhere. Careful study for allergy will show that the patient is sensitive to one or more of the foods in the diet.

3. *Complications*.—Although the ulcer diet may relieve the pain in pyloric stenosis, the delayed vomiting will continue if the lumen is too small to permit the easy and rapid egress of the food. Partial perforation, with marked infiltration of the wall and adhesions to neighboring organs, not only will tend to produce obstructive symptoms, but due to the fact that it prevents healing of the ulcer will cause persistence of ulcer symptoms for long periods of time. Ulcer symptoms which are wholly or partially relieved by diet but which always recur when the diet is neglected are usually caused by this complication, which requires operation for a cure. More distant complications in the gastrointestinal tract, such as cholecystitis, appendicitis, and colitis, or outside of the tract, such as pelvic, genitourinary, or cardiovascular diseases, also may cause symptoms which an ulcer diet will not relieve. It is therefore imperative, before instituting treatment for ulcer, to make a complete survey of the patient and thus avoid embarrassing discoveries later.

#### COMPLICATIONS

The complications of ulcer except acute perforation all may be favorably affected by dietary measures. In *stenosis*, pyloric or hour-glass, the narrowing may at times be due only to an acute inflammatory reaction with edema and spasm, and may be promptly relieved by rest and the use of frequent small, liquid feedings. But even in a definite, tight cicatricial stenosis the patient often presents himself in a condition in which immediate operation would be extremely risky. There may be acidosis, alkalosis, or hypochloremia and the general bodily nutrition is usually at a low ebb. An adequate and balanced liquid diet, fortified with parenteral feedings, will be of great help for these conditions. The stomach wall is usually so stretched by overdistention with food that it is difficult to estimate the required size of the gastroenterostomy stoma, and its muscular tone is so poor that after operation peristalsis is delayed and weak, accounting for many of the poor results in these cases. Frequent small feedings will usually cause a marked reduction in the size of the stomach and a restoration of the tone of its musculature. The intestinal tract distal to the obstruction, having become accustomed to little if any reception of stomach contents, becomes sluggish and atonic, its secretions are diminished, and a sudden influx of food after a gastroenterostomy will usually produce symptoms popularly classified under the heading of gases, but really due to definite motor and secretory disturbances. A routine, such as that given below, practiced for a period of ten days or two weeks preceding operation, or up to the point where the patient obviously ceases to improve in weight and general condition, has reduced our mortality following operation in stenosis practically to nil.

## ROUTINE IN STENOSIS CASES

1. Complete bed rest is essential, to reduce caloric requirements and to prevent intra-abdominal irritation.

2. Acidosis or alkalosis, dehydration, and hypochloremia may require occasional parenteral administration of glucose and saline solutions.

3. Frequent small feedings of one of the following formulas will provide nourishment and physiologic stimulation of peristalsis and secretion. In marked dilatation, four ounces every two hours should be the dose at the start, with aspiration of stomach residue once or twice in twenty-four hours to see whether the stomach is expelling all of the feedings. Usually it can be increased to six or eight ounces every two hours, with an added raw egg three times daily, and the juice of an orange at the end of a feeding twice daily.

4. Roentgen-ray check-up at the end of ten days or two weeks will disclose whether the desired effect has been obtained and, in the cases with temporary causes for the obstruction, will show perfect emptying.

The diet formulas used in these cases are as follows:

## STENOSIS MIXTURE

All mixtures should be palatable. Nurse should taste them before giving to patients. Flavoring may be added.

	Amount	Carbo- hydrate	Protein	Fat	Calories
Glucose	60 gm.	60			240
Cream (20%)	120 c.c.	4	4	24	240
Milk	880 c.c.	35	25	25	550
		<hr/>	<hr/>	<hr/>	<hr/>
		99	29	49	1,000 (approximately)

This formula to be supplied by diet kitchen every twenty-four hours, kept in refrigerator, served cool (not cold) or warm.

## GELATIN-MILK MIXTURE

	Amount	Carbohy- drate	Protein	Fat	Calories
Gelatin	30 gm.		27		100
Glucose	60 gm.	60			240
Cream (20%)	100 c.c.	3	3	18	180
Milk	900 c.c.	36	27	27	550
		<hr/>	<hr/>	<hr/>	<hr/>
		99	57	45	1,000 (approximately)

This formula to be supplied by diet kitchen every twelve hours, kept cool, but not in refrigerator, to prevent jelling, and served cool or warm.

It will be noted that both mixtures provide 1,000 calories per liter, making it easy to compute the value of a given diet. The formulas are also useful for feedings through a stomach tube. Both mixtures are palatable in themselves, but they are sweet and may be improved by the addition, at the time of the feedings, of such flavors as chocolate, vanilla, coffee, or tea.

In *gastric hemorrhage* the bleeding proceeds either from a bleeding vessel at the base of the ulcer or from capillary oozing. In either case certain indications present themselves.

The bleeding area requires special attention. It must be realized that a stomach full of blood aids in the checking of a hemorrhage, but when vomiting occurs and when the stomach empties itself normally, hunger contractions will occur. These contractions are rhythmic in type, alternating with relaxation, thus causing frequent changes in tension at the site of the bleeding, tending to cause its prolongation or recurrence. The presence of the blood also stimulates gastric secretion, which may digest the clot and the edges of the bleeding area. It is therefore desirable, in order to avoid these hunger contractions and this undesirable digestive effect, to put something into the stomach which will produce the slower, less forcible peristaltic waves and which will combine with the gastric juice, without overstimulating it. This substance should also be soothing, should, if possible, encourage coagulation of blood, and should be administered in sufficient quantity and with sufficient frequency to accomplish the desired effects.

Gelatin is a substance which is ideal for the purpose just mentioned. In addition to this it is a protein food, loses none of its coagulant properties when diluted, and prevents the formation of large curds in the digestion of milk when used in combination. A mixture<sup>1</sup> of gelatin, glucose, water, and fruit juices has been used by me for over twenty years with good effect, and in the past few years has been superseded by the gelatin-milk mixture described above. The diet routine is as follows:

#### FEEDINGS AFTER GASTRIC HEMORRHAGE

For patients immediately after hematemesis

No feedings while patient is asleep

No ice, water, or other drinks to be given

*Gelatin-milk mixture* to be given cool or warm, as follows:

1st and 2nd days: 4 oz. every 1½ hr.

3rd, 4th, and 5th days: 5 oz. every 2 hr.

6th and 7th days: 6 oz. every 2 hr.

Now add to each of four feedings one of the following:

1 soft boiled or poached egg

3 ounces of cereal

Custard, jello, or ice cream

8th and 9th days: As above, only add 2 extras to each of 3 feedings

10th day and thereafter: Ulcer diet

Water, beginning on 5th day, increasing amounts, starting with

1 oz. at a time

Mineral oil, ½ oz. each night, beginning on second night

Iron and vitamin preparations as indicated

Shock, present in all severe hemorrhages, is the first alarming symptom to be treated, and the standard treatment of complete rest, ap-

plication of warmth to the body, and the hypodermatic administration of morphine is indicated.

The lowered blood pressure caused by the hemorrhage and aiding in the cessation of bleeding by permitting clots to form at the site of bleeding is therefore really a life-saving mechanism and should not be overtreated. Usually no stimulation is required and parenteral administration of fluids should be avoided, as the tendency to sudden raising of the blood pressure often produces a new hemorrhage, even where blood is used. Many such patients die as a result of transfusions.

Severe anoxemia, as indicated by air hunger and a very weak, thready pulse, may be considered an indication for the slow addition of a small amount of blood to the circulation. The transfusion should be stopped as soon as the symptoms subside and not more than 200 c.c. should be given at one time.

Anemia, even though marked, is not in itself an indication for transfusions. I have seen patients with hemoglobin as low as 12 or 15 per cent who did very well without transfusion, but after a week or ten days, when the danger of causing a recurrence of bleeding is over, I frequently resort to larger transfusions to shorten the period of convalescence. Iron and vitamin preparations may be given by mouth with the feedings almost from the start. In most cases no further antianemic therapy is required.

Impaired blood coagulability, as shown by suitable tests, may be treated by the use of coagulants, by intramuscular injections of heterologous blood, or by the administration of the new vitamin K.

Constipation is not an important symptom, and no effort should be made to induce defecation for at least three or four days. Then an oil retention enema followed by a small rinsing enema is all that is required. Mineral oil by mouth may be used as a routine.

This routine in hemorrhage has resulted in a decrease in mortality in a recent series of 84 cases to less than 6 per cent, 2 of the 4 cases dying (being moribund on admission) and the other 2 showing at autopsy large bleeding vessels held firmly open by thick, horny, friable tissues surrounding an old perforation. All of these patients had also received intravenous injections on admission, contrary to the usual orders. My patients are comfortable, are satisfied with their food, and regenerate blood very rapidly even without the addition of iron, although this is usually used. Meulengracht<sup>2</sup> has only recently called attention to the desirability of early feedings after hemorrhage and has shown excellent results by giving a much more liberal and more irritating diet than mine, but I feel that my more conservative diet, which is nutritious and well-balanced and sufficiently satisfying to the patient, is to be preferred.

One more topic of interest to surgeons is that of diets after operation<sup>3</sup> for ulcer. For nearly twenty years I have made it a practice to

feed my postoperative patients as soon as the operation is completed, if a local anesthesia is used, and as soon as they can swallow, when general anesthesia has been administered. My routine has been practically the same as in my hemorrhage cases. The result has been that early peristalsis has been instituted, resulting in almost no vomiting or distention and usually in spontaneous bowel movements beginning the third or fourth day. Meanwhile the patient is getting sufficient fluids by mouth, is being given nearly 1,500 calories of food the first day after operation and more thereafter, and rarely requires more than one or two intravenous or subcutaneous fluid injections. The result is a happy patient who shows no untoward effects from the operation and is grateful for the experience.

I hope that I have shown how careful attention to diet in ulcer patients will result in more comfort to the patient, more rapid healing of the lesion, and less worry to the attendant.

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# PERFORATION OF CARCINOMA OF THE STOMACH\*

## REVIEW OF THE LITERATURE AND REPORT OF CASE

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**P**ERFORATION would appear to be an uncommon complication of carcinoma of the stomach. Such a conclusion, based upon personal observation, is further borne out by the paucity of reports in the literature. Perforation of gastric ulcers occurs in about 5 per cent of cases, but the incidence of perforation of carcinoma of the stomach is not a matter of record; obviously it must be low.

This condition was first described by Laennec over one hundred years ago. Reference to it in American medical literature is infrequent; reports in foreign publications are a trifle more common. Evidence of the clinical recognition of the condition is noted in the case records of the Massachusetts General Hospital in the years 1932,<sup>1</sup> 1934,<sup>2</sup> and 1936.<sup>3</sup>

In 1935 Aird<sup>4</sup> reviewed the literature, reporting 1 case of perforation from his own practice, 7 cases from the Royal Infirmary of Edinburgh, and 71 cases from the literature. Aird concludes from his studies that either the complication is most uncommon or is rarely recognized. He has divided the cases into four groups clinically. Group 1 comprises the cases with sudden onset accompanied by the typical signs of perforation, as seen in peptic ulcer, and with a history of previous indigestion. The cases of Group 2 are similar to these except for the absence of a history of previous indigestion. In Group 3 are the cases with slow leakage and symptoms comparable to those occurring with subacute perforations of benign ulcers. The cases in Group 4 have no localizing symptoms at all; there may be a spreading peritonitis with no apparent cause. More than two-thirds of the reported cases fall in Groups 1 and 2.

It is interesting to review the case reports in the literature. In many instances the histories were of no help in making a diagnosis. Some patients did give a history of indigestion of many years' duration; the peculiar thing was that the indigestion was not typical of ulcer, being uninfluenced by food or alkali in so many instances. In the personal case reported by Aird,<sup>4</sup> there was a history of epigastric pain of some years' duration, unrelated to food. In the case reported by Brunswick and Heinz<sup>5</sup> in 1936 there was a history of stomach trouble of ten years' duration. Likewise in the case I am about to report there

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was a similar history of more than ten years' standing. Such facts open up a field for speculation. Our opinion in regard to malignancy arising in a pre-existing benign peptic ulcer has undergone some changes in the past decade. Whereas we used to feel that a fairly high percentage of gastric cancers had their origin in pre-existing ulcers, the present concept seems to be that this is true in a very small percentage of cases (certainly less than 10 per cent). These patients with perforated malignant ulcers often give a history of very long standing stomach trouble as is noted above; further, this history is usually not that of the typical peptic ulcer. However, based upon the duration of the symptoms, it must be assumed that such ulcerations are benign in the beginning. What then are the factors which result in the transition to malignancy? This question will have to await the answer of a research worker. What if any symptoms warn us of this transition? This is our problem as clinicians. Careful observation and repeated x-ray examinations constitute the answer. Any patient with symptoms of peptic ulcer who does not show definite improvement clinically with strict ulcer therapy and whose repeated x-rays do not show some evidence of healing after one month should be regarded with suspicion. If this lack of improvement persists for another four weeks, then exploration with a view to resection is certainly indicated.

As has been implied, a correct preoperative diagnosis in cases of perforation of carcinoma of the stomach rarely has been made. What is more astonishing is that the correct diagnosis usually has been missed at operation. In my own case the operative findings in retrospect would strongly suggest the correct diagnosis, yet I passed them up merely emphasizing the widespread induration and the difficulty in closing the perforation. Aird<sup>4</sup> comments upon the difficulty of closing the perforation because of the friability of the stomach wall.

In the case recognized at operation, what shall be our treatment? Ideally resection is indicated. Many of these patients are in poor condition, however, due to prolonged stomach trouble and the acute episode of perforation. Many of them will stand the minimum of surgery only. The mortality rate approaches 50 per cent. So it would seem that the primary operation should be limited to closure of the perforation, reserving resection for a later time when the patient is better able to withstand it.

The following case is recorded because of the comparative rarity of reports of perforations of gastric cancers. There is a history of indigestion of ten years' duration, pain unrelieved by taking of food, progressive loss of weight and strength and secondary anemia. The case demonstrates the missing of the diagnosis both before and at operation.

CASE REPORT.—W. V. E., a male farmer, aged 49 years, was admitted to the Memorial Hospital on June 7, 1937, complaining of severe abdominal pain of four hours' duration. He had vomited twice since the onset of the pain. He gave a history of stomach trouble and progressive weakness of ten years' duration. He stated that when he worked hard he would suffer with pain in the stomach and bloating; if he did not work hard, he had no trouble at all. The pain was unrelieved by taking of food but saleratus and peppermint would "break up the gas," as he expressed it. During intervals between attacks, he was able to eat anything without distress. Gradually the attacks became more frequent and were brought on by less exertion. Occasionally he would vomit with the attacks. He never noticed any blood in the vomitus, which was like thick saliva, nor were the stools dark colored at any time. Six months before this admission, he noticed he was much worse; he commenced to feel shaky and his heart would beat fast with any exertion. The attacks of pain in the stomach and bloating now came on every day. He then consulted his physician who made a working diagnosis of peptic ulcer and placed the patient on a Sippy regime and also a hematinic. Under this treatment there was some improvement. The present attack commenced like the previous ones but did not yield to the usual saleratus. Before admission to the hospital the patient had received 0.5 gr. of morphine sulfate with no relief. The patient was admitted in moderate shock; the temperature was 97.4; the pulse, 82; respirations, 20. The patient looked pale and sick. The abdomen was retracted and boardlike; no peristaltic waves were heard; there was tenderness in the epigastrium and right lower quadrant. The heart and lungs were essentially negative. The admission blood count was as follows: red cells, 3,360,000; hemoglobin, 59 per cent (Hellige); white cells, 12,280; neutrophils, 85 per cent; lymphocytes, 11 per cent; endothelial cells and eosinophiles, each 2 per cent; the smear showed moderate variation in size of the red cells, slight variation in shape, and slight polychromatophilia.

A tentative diagnosis of perforated peptic ulcer was made and the patient was prepared for operation by external heat and intravenous injection of 1,000 c.c. of 5 per cent glucose in saline; he was also grouped and cross-matched for transfusion. At operation, about two hours following admission, the abdomen was explored through a long right rectus incision. There was considerable flocculent free fluid in the peritoneal cavity (cultures were negative). The entire pyloric area was greatly indurated and the serosa of the pylorus was more roughened than usual. There was a perforated ulcer on the anterior wall just proximal to the pylorus. No enlarged glands were noted. The ulcer was cauterized with the actual cautery. Attempts at closure of the ulcer by suture failed because of the great friability of the stomach wall. "A blow out" patch of omentum was then sutured across the perforation and the abdominal incision closed with one cigarette drain in the upper quadrant and another in the lower right quadrant emerging through a stab wound below. The post-operative course was not remarkable. The patient was supplied with fluids by the intravenous route until the fourth day when water was allowed by mouth. Later he was placed on a liquid Sippy diet and in a few days the usual powders were added. A blood count on the fourteenth postoperative day showed 4,000,000 red cells and 60 per cent hemoglobin. On the nineteenth day he was discharged from hospital feeling quite good and with no stomach distress.

After discharge from hospital he was under the care of his family physician who had followed the patient's course carefully while in hospital. The patient continued with a strict Sippy diet, including powders, and also was given liver for his anemia. Recovery of strength was slow after operation, but the patient resumed work about six weeks following discharge from hospital. In spite of a careful diet he still "bloomed" after each meal but there was no real pain. He did not vomit and the



stools were not dark colored. About two weeks before his second admission, he noticed that he was "weaker than water" and could not do any physical work; about this time he started to have pain in the stomach. It was unrelieved by anything he took, was constant day and night, and prevented him from getting much rest.

On Oct. 6, 1937, four months after the original admission, the patient was readmitted complaining of pain in the stomach and weakness. He looked pale and anemic. The admission temperature, pulse and respiratory rates were normal. The admission weight was 124 pounds in contrast to 130 at the time of the first admission. The physical examination showed little except tenderness in the epigastrium. No mass could be made out. No enlarged lymph nodes or rectal shelf were noted. The red cells numbered 3,070,000; hemoglobin, 42 per cent (Hellige); the white cells, 4,080 with 73 per cent neutrophils, 24 per cent lymphocytes, 2 per cent endothelial cells, and 1 per cent eosinophils. There was marked variation in size and shape of the red blood cells with moderate achromia. X-ray examination and fluoroscopy showed a constant narrowing of the distal 4 cm. of the stomach with hypermotility; this, with other findings, led to the x-ray diagnosis of carcinoma of the stomach. A subtotal resection of the stomach was advised and accepted by the patient. For this he was prepared by multiple transfusions of 500 c.c. each. On the fourth day, operation was performed. The pyloric portion of the stomach was hidden in adhesions and densely bound down to the liver. As one felt of this area, it conveyed the impression of a mass about the size and shape and consistency of a golfball. There were a few small, soft lymph glands along the greater curvature, but none were noted on the lesser curvature and no metastases were found in the liver. A Polya type of resection with closure of the duodenal stump and anastomosis between the cut edge of the stomach and the side of the jejunum was done. This was rendered very difficult on account of the many adhesions. However, a satisfactory union was accomplished and the abdominal incision closed by layer. Following operation, the patient did poorly and in spite of all measures used to combat the existing shock died a few hours after completion of the operation. We were unable to obtain a post-mortem examination.

The pathologist's report is as follows: "A segment of stomach measuring 13.5 by 13 cm. It apparently represents the incised pyloric end of the stomach although the pylorus cannot be identified because of the large neoplastic mass. This is observed on the mucosal surface. Here there are two large, circular lesions separated by a narrow strip of mucosa about 1 cm. in width. Each lesion is roughly circular with elevated margins composed of gray granular tissue. They probably represent a single lesion cut through when the stomach segment was opened. Distal to the mass there is a segment of grossly uninvolved stomach measuring 2.5 cm. in length and proximally uninvolved stomach measuring 5 cm. The neoplastic mass measures roughly 8 by 10 cm. Its margins rise 1.5 to 2 cm. above the mucosal surface. Grossly the neoplasm has destroyed the muscle and extended into the serosal fat. The fatty mesentery contains a few moderately enlarged lymph nodes which present gray granular areas." The microscopic description is omitted. The diagnosis was adenocarcinoma of the stomach with chronic lymphadenitis.

#### CONCLUSIONS

1. Perforation of carcinoma of the stomach is quite unusual.
2. The condition is rarely recognized before operation and seldom at operation.
3. The mortality rate is about 50 per cent.

4. The majority of cases of perforated carcinoma of the stomach give a history of sudden onset accompanied by the typical signs of perforation of a peptic ulcer. Usually there is a history of indigestion of long standing.

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# OBLIQUE, ASEPTIC, END-TO-END INTESTINAL ANASTOMOSIS

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## INTRODUCTION

THE VOLUMINOUS annual literature on intestinal anastomosis stands as evidence that a satisfactory procedure has not been evolved. Parker and Kerr<sup>1</sup> pointed out that at the time of their publication some two hundred methods and literally thousands of papers on the subject had appeared.

I have had occasion to perform anastomoses on dogs in the course of Thiry-Vella fistula formation.<sup>2</sup> For this purpose, the criteria of a satisfactory anastomosis were found to be that it should be quickly and easily done; that it should be aseptic; that it should be nonobstructive, either during the stage of postoperative edema or after contraction of the scar has occurred; and finally that the area of anastomosis function as nearly physiologically as possible, without ballooning just above it, without outpocketings, and without angulation of the gut.

In a number of dogs the method of Martzloff and Burget<sup>3</sup> was used. With this method there was no difficulty with contamination or perforation, but in the author's hands obstructive symptoms appeared if the animals were placed on regular food within five to seven days. Provided the dogs were kept on liquids and given subcutaneous injections of 0.9 per cent sodium chloride as indicated, they recovered apparently normal intestinal function in ten days to two weeks. Post-mortem examination of such anastomoses revealed marked stenosis at the site of suture and ballooning of the gut immediately above.

One procedure was done with inversion of both ends and open side-to-side anastomosis. The postoperative course was excellent, and the dog had returned to his usual diet within two days, but the method was more laborious and time-consuming than seemed necessary.

The lateral anastomosis of Soresi<sup>4</sup> would perhaps have offered an answer, but it is open to the reasonable objection that it is not an aseptic procedure. Also, the diagonal end-to-side anastomosis of Collins<sup>5</sup> probably could be used for this purpose, though it was evidently intended for ileocolostomy, but it is a more complicated procedure and there is some angulation of the bowel incident to it.

The end-to-end anastomosis, using a temporary basting stitch for closure of the ends while they are being sutured together, which was devised by Parker and Kerr, was tried, but closure with one layer of

interrupted sutures proved inadequate and some leakage occurred, with resultant adhesions to other loops of small intestine. An additional layer of sutures would seem necessary to prevent this. The method I use has the advantages of involving one less step, turning in less bowel, and leaving no angulation in the gut, even when distended. In the article cited, Parker and Kerr grant that, even after complete healing has occurred, the bowel on moderate distention has an angulation of about  $160^{\circ}$ .

The Rankin method of anastomosis<sup>6</sup> also was tried. With an instrument of smaller caliber, this might be feasible in the dog, but the standard Rankin instrument is too large for small intestinal anastomosis in the dog and offers no advantages over the instrument of Martzloff and Burget.

Gatch<sup>7</sup> described a method of aseptic end-to-end anastomosis which he used on the small intestine of dogs. This consisted in a procedure similar in principle to that previously described by Parker and Kerr. It seems to me to be open to the objection that inversion of an unnecessarily great flange of tissue at the suture site results, a danger mentioned by Parker and Kerr. All but one of Gatch's eighteen dogs recovered, but no data were given concerning the readiness with which a normal diet was resumed.

W. S. Halsted in 1922<sup>8</sup> reported a method of "blind-end circular suture of the intestine, closed ends abutted and the double diaphragm punctured with a knife introduced per rectum." This almost ideally aseptic procedure was highly successful in his hands in the colon of the dog, but its application to various levels of the ileum would be difficult. This method is also open to the objection that a large flange is inverted at the suture line. This partial diaphragm was probably of no importance in Halsted's experiments because they were almost entirely confined to the large intestine.

The method of Furniss<sup>9</sup> also was tried. Contrary to the claims of that writer, I experienced great difficulty in sites in which the ends to be anastomosed differed greatly in diameter. The instrument was too large for the small intestine of the dog and appeared to have no advantages over that of Martzloff and Burget.

It is because of the shortcomings of these methods that I venture to present a method which in my hands has proved highly successful.

#### TECHNIQUE OF THE ANASTOMOSIS

The oblique, aseptic, end-to-end anastomosis with rotation is a modification of the method of Martzloff and Burget, incorporating also some of the features of the Parker-Kerr procedure. Sites of section are chosen such that the blood supply to the suture line is maximal; these areas are freed of mesentery and fat after ligation of the vessels with fine silk, and the mesentery is split almost to the root. Long, slender, longi-

tudinally grooved, crushing clamps like those of Burget and Martzloff and like those of Parker and Kerr are employed, but they are placed at an angle of 30 to 40° from the long axis of the bowel, the mesenteric angle being acute and thus longer than the antimesenteric. On one of the ends to be anastomosed, the crushing clamp is placed with the joint of the instrument at the antimesenteric border; on the other end the joint of the clamp is at the mesenteric border. At each end a denuded area about 5 mm. long is left between the ligated vessels of the mesentery and the crushing clamp. Two Kocher forceps are placed on the bowel between the clamps just described and about 1 mm. from each of them. The bowel is cut between each pair, and the four cut ends are phenolized, alcoholized, and dried.

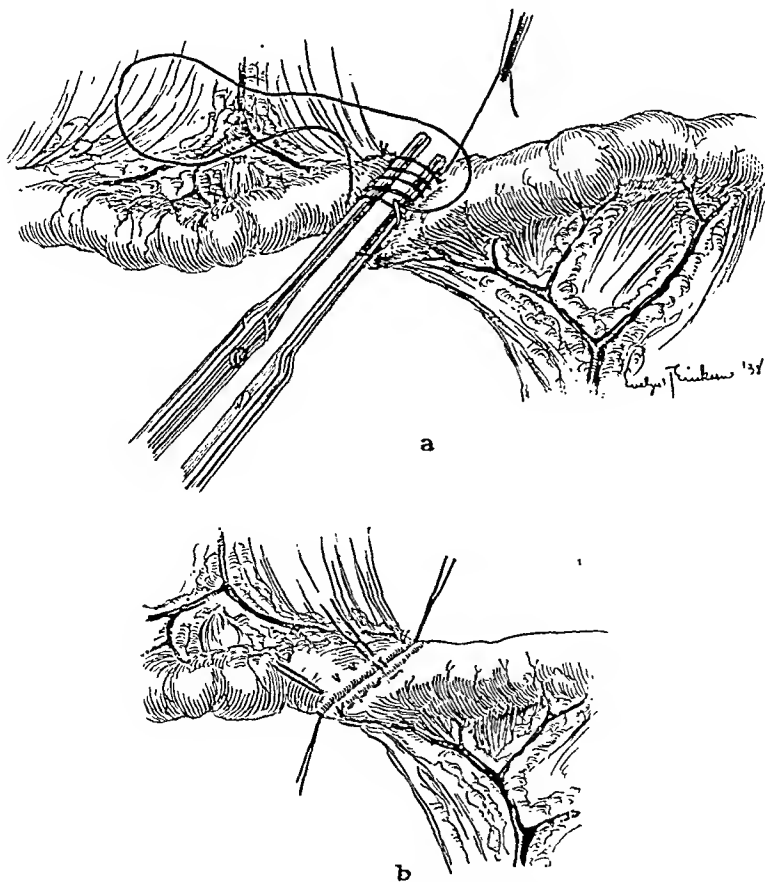


Fig. 1.—a, Approximation of the ends to be anastomosed, after 180° rotation of one segment. A running suture of plain catgut is laid on either side of the very obliquely placed narrow crushing clamps. The drawing shows placement of the first of these two running sutures. b, Insertion of Halsted mattress stitches after removal of clamps and inversion of the crushed areas by the use of the running catgut suture.

For the purpose of establishing the Thiry-Vella fistula, the ends of the loop are at once removed from the abdomen through two stab wounds made in the left flank.

The ends to be anastomosed are now approximated in such fashion that the crushing forceps lie side by side; that is, so that the mesenteric border of the upper end is apposed to the antimesenteric border of the lower end, and vice versa for the other borders, as shown in Figure 1 *a*. A running suture of 00 or 000 plain catgut on a fine curved needle is started without tying at one border about 2 mm. back from the clamp, and bites about 4 mm. long are taken on alternate sides of the two apposed clamps; that is, alternately on the two ends to be anastomosed, as shown in Fig. 1 *a*. When the length of the clamps has been covered in this fashion, the bowel is turned over and a similar suture is laid on the opposite side. These two sutures, one on either side of the bowel, are held taut while an assistant cautiously loosens and removes the two clamps, the crushed area inverting as the instruments are removed. After inspection to be sure inversion is complete, the loose ends are tied just tightly enough to maintain apposition of the serosal surfaces but not tightly enough to constrict the lumen, and a second line of sutures is laid, interrupted Halsted mattress sutures of fine silk, as recommended by Martzloff and Burget and as shown in Fig. 1 *b*. Care must be taken not to include tissue deeper than the submucosa in either of these layers of stitches. The mesentery is now closed, the anastomosis is loosely covered with omentum, and the whole is replaced into the abdomen.

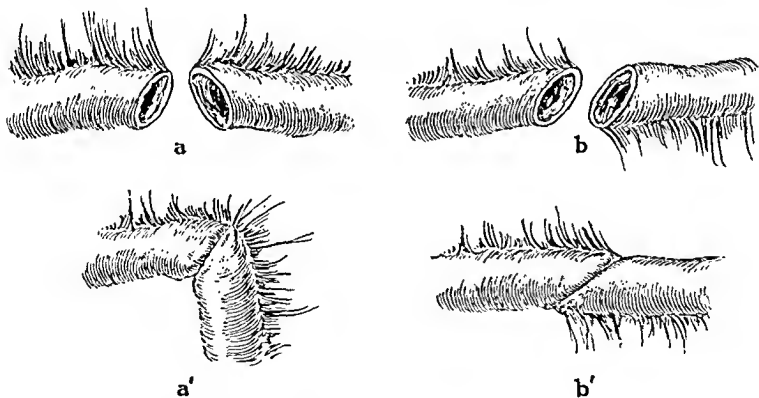


Fig. 2.—*a*, Diagrammatic demonstration of the angulation which follows anastomosis after oblique section without rotation. *b*, Diagrammatic demonstration of absence of angulation or outpouching if rotation precedes the above anastomosis.

Nine anastomoses have been made in this fashion, and difficulty has been encountered with symptoms of obstruction in one animal alone, in which one of the silk sutures was carelessly placed so as to include some of the opposite wall of the bowel. Food is offered two days after operation, and the usual amount for the animal is ordinarily taken on the fourth day postoperatively. Intraperitoneal sodium pentobarbital, 35 mg. per kilogram of the dog's weight, has been used exclusively for anesthesia.

## DISCUSSION OF TECHNIQUE

In view of the fact that Martzloff and Burget did end-to-end anastomoses with narrow crushing clamps and essentially the technique here described, and inasmuch as Parker and Kerr placed their clamps on the bowel at an angle of approximately  $45^\circ$ , the mesenteric border being the longer, the only real innovation in my method is the rotation through  $180^\circ$  of one of the segments to be anastomosed, as pictured in Fig. 1. The value of this rotation is illustrated in Fig. 2. Here it will be seen that if the two ends are cut at about  $45^\circ$  and anastomosed with mesenteric border to mesenteric border, a marked angulation necessarily results (Fig. 2 *a*). Parker and Kerr grant that even after healing has occurred there is still an angulation of  $160^\circ$ , with a funnel-shaped depression in the gut wall on the mesenteric border; in all probability there is even greater angulation shortly after operation when edema is present. With my method, diagrammed in Fig. 2 *b*, the  $180^\circ$  rotation does away with the possibility of such angulation on the one hand, and in addition should be more physiologically correct inasmuch as all the fibers which are cut, both circular and longitudinal, are anastomosed to similar fibers in the other bowel end, a point the importance of which has been stressed by Collins. Thus, there are left no circular fibers without attachment, as would be the case near the mesenteric border in the anastomosis pictured in Fig. 2 *a*. This should prevent the development of outpouchings, such as the funnel-shaped depression described by Parker and Kerr.

This method is advantageous in that it is quickly and aseptically done and, by virtue of the oblique line of suture, offers a minimum of stenosis even in the presence of postoperative edema. One animal died of other cause on the third day postoperatively; here there was no narrowing of the lumen in spite of edema. Another died two weeks after operation due to the carelessly laid stitch already mentioned which occluded the lumen; even in this case the mucosa had healed so that the suture line was marked only as a hairline scar. Two dogs were sacrificed four weeks postoperatively. In one of these, after fixation in formalin, the circumference internally at the line of suture was 4 cm.; measured along the slightly elevated scar it was 3.8 cm.; four cm. above the anastomosis it was 3.4 cm. and four cm. below it was 3.2 cm. In the other, the corresponding figures were 2.7 cm., 3.4 cm., 2.6 cm., and 2.4 cm., respectively. The absence of constriction or ballooning at the site of anastomosis is evident.

Some complications perhaps might be expected from the rotation because of the resulting abnormal position of the mesentery, but no difficulty whatsoever thus far has been observed. The final position corresponds rather to rotation of each segment a quarter turn than to rotation of one end only.

## CONCLUSION

A method of oblique, aseptic, end-to-end intestinal anastomosis with 180° rotation of one of the bowel ends has been presented which is advantageous in simplicity of performance, in absence of late stenosis, and in the absence of early obstructive symptoms which usually result from edema with circular methods.

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## THE UTILIZATION OF DOGS IN EXPERIMENTAL PROCTOLOGY

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THE art of surgery cannot be mastered in the lecture room. Only fundamental principles are taught. But sound surgical judgment, the spearhead of a seasoned surgeon, is predicated upon knowledge, experience, and confidence; surgical ability is founded upon skill and dexterity.

These postulates are obvious and their relative merits need not be stressed. However, their attainment may be greatly expedited by acquiring and developing proper surgical technique in addition to other forms of training. To quote in this connection Partipilo, who states: "The ideal surgeon must not only be a good operator, but also a master technician. He must be on the alert and be ready to meet unexpected conditions, make quick decisions, and finally execute an operative procedure with poise and calmness. There are many surgeons possessing many good qualities who operate clumsily and awkwardly because they have not developed manual dexterity. At times this may be due to lack of natural aptitude; more often it is due to insufficient training. The movements of a dextrous surgeon are agile, purposeful, rhythmical, and apparently executed without effort or exertion."

Laboratory experimentation on dogs and other animals has been fundamentally responsible for the many advances made in surgery in the past fifty years. Yet, despite the accomplishments in every other field of surgery, nothing has been done to render anorectal surgery on the experimental dog a reality and to apply the same reasoning and principles to this phase of proctologic training. Progress in proctology can be attributed largely to the many notable contributions of illustrious and inspiring investigators. Training of students for this specialty has been confined entirely to apprenticeships with competent proctologists, or to courses offered in a few graduate schools, without the valuable aid of practical work on the dog. However, refinements of technique, the development and solution of many intricate problems, and the teaching of the art of proctologic surgery can be much enhanced by practicing dog surgery.

### ANATOMY

The dog lends itself admirably to proctologic surgery and every conceivable type of operation may be performed with superb realism. Of course, the anatomy of the dog differs somewhat from that of the human,

yet we find it suitable for study purposes in this field. The rectum of the dog is approximately a straight tube, being a continuation of the colon, and ends in the anus. Externally, the tube is even and shows the course of the longitudinal muscle fibers. Unlike the human, it is freely moveable and is suspended from the middorsal line by a narrow mesentery (mesorectum), which is continuous with the mesocolon. Its dorsal surface is covered with peritoneum which slopes obliquely across the lateral surface of the tube in such a manner that the ventral surface has scarcely any peritoneal investment. It is surrounded by the internal sphincter which is merely a thickening of the circular fibers of the muscle of the rectum. It is supported by the rectococcygeus muscle, formed by the longitudinal muscle fibers of the rectum on its outer aspect and medially to it by the levator ani. This latter muscle is relatively broad and thin, triangular in form, lies laterally to the rectum and anus, and arises from the anterior border of the pubis and from the medial surface of the ileum. Some of its fibers blend with the external sphincter and some end on the third and fourth vertebrae of the tail. This muscle, together with the coccygeus, forms a kind of pelvic diaphragm, pierced by the alimentary and urogenital canals.

The anus, the terminal opening of the intestine, is surrounded by thick skin, provided with a somewhat scanty supply of short, fine hairs. Leading to the anus is the para-analis recti, the lining of which has been described as divisible into three zones: (1) The zona cutanea, which is continuous with the skin outside the anus (perianal region) and shows on each side a small opening leading into a sac, from a hazelnut to a walnut in size, known as the para-anal sinus (sinus para-analis). The sinus lies between the external sphincter muscle of the anus and the longitudinal muscle of the rectum and has a lining membrane furnished with glands that produce a thickish, strong smelling secretion. (2) A narrow and indefinite zona intermedia separates the cutaneous zone from (3) the zona columnaris, in which there are folds of mucous membrane, mainly longitudinal in direction (at the pectinate line). At this point there is a fine line of demarcation analogous to the pectinate line in the human, possessing valvelike structures, covered with a thin membranous epithelium, slightly pigmented a dark brown, through which a small hook may be introduced. It is here that the folds of mucous membrane described above project, resembling very much the columns of Morgagni in the human (crypts in dog).

The anus is surrounded and supported by the external sphincter muscle, a ringlike structure, which is connected dorsally with the aponeurosis of the tail, and ventrally by some of its fibers to the bulbos urethrae. A pale band of muscular fibers, separated from its fellow by the middle coccygeal vessels, arises from the bodies of the first and second (and possibly third) coccygeal vertebrae. Some of the fibers end, under cover of the sphincter ani, on the para-anal sinus; while others are

continued ventral to the anus to become the retractor muscle of the penis. In the female the description applies except that ventrally, the rectum is related to the vagina and vestibule.

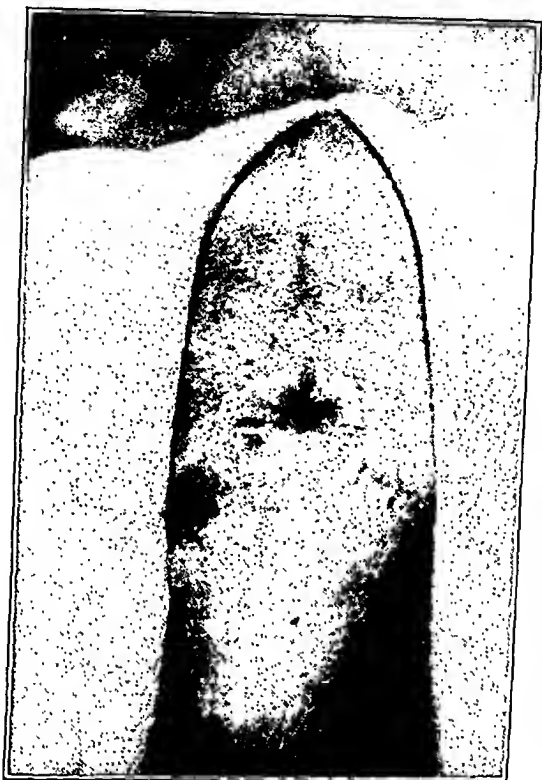


Fig. 1.—Lithotomy position. The dog lies on his back, the hind legs being tied to the forelegs; tail firmly attached over the edge of table, the region shaved and draped.

#### SCOPE OF STUDY

It can be seen from the anatomy of the dog that there is sufficient resemblance in these structures as compared to the human being to make this animal suitable for proctologic study in operative surgery. We have found it possible to produce prolapses of the entire wall of the rectum to closely simulate a human procidentia recti, upon which the various types of resection may be performed. The sinuses in the perianal region serve a dual purpose: an ischioanal abscess and horseshoe fistula. The redundant mucosa permits the performance of a simple and the amputative type of hemorrhoidectomy. We can demonstrate the various surgical procedures for external thrombotic hemorrhoids, pruritus ani, fissure, cryptitis, and fistulas. Sphincterotomy, proctotomy, perineal and abdominal-perineal resection, and injection treatments for internal hemorrhoids and pruritus ani are performed.

Although the tube is devoid of structures normal to the rectum and sigmoid of the human being, the practice in the use of the sigmoidoscope and anoscope and the proper method of introducing and passing, as well as repeatedly observing the normal appearance of mucosa, is extremely profitable.



Fig. 2.—Dog in inverted position, the hind legs being firmly attached to opposite side of table. Forelegs are not fastened. Usual draping and tray of instruments shown.

#### POSITION AND PREPARATION

After the dog has been anesthetized (the use of sodium amytal for premedication has been found to be invaluable and eliminates complicated anesthetic procedures), it may be placed in one of two positions, the lithotomy or the inverted. In the beginning we employed the lithotomy (Fig. 1) but later found the inverted position to be far more satisfactory. The dog is placed ventrally (Fig. 2) with its head down, resting on a board leaning against the operating table at an angle of 75 degrees. The legs are stretched across the top of the operating table and fastened. The forelegs may be attached to the board. The tail is fastened to the skin of the dog by towel clips. In order to avert sudden death, ether must be administered cautiously to the dog; and, further, it should not be placed in the inverted position until ready

for use. The entire region around the anus is shaved and cleaned, towels applied in exactly the same manner as in the human being, and covered with a small sheet (Fig. 3).

#### MODUS OPERANDI

A digital and bidigital examination is made, followed by anoscopy and sigmoidoscopy. The para-anal glands give the impression to the palpating fingers of soft, fluctuating masses similar to ischioanal abscesses. When the contents of the sinuses are thoroughly squeezed out, one perceives a fibrous tract, characteristic of a chronic fistula.

The rectum being a straight tube, there is no difficulty passing the sigmoidoscope. However, an opportunity is afforded to apply the practical and essential features of the procedure, to stress the dangers of general anesthesia, and to demonstrate the important maneuvers necessary to a successful sigmoidoscopic examination.

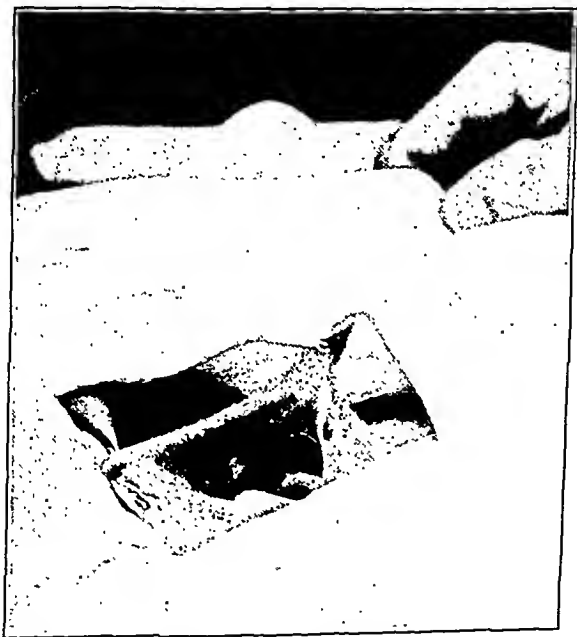


Fig. 3.—Close-up view of draped dog.

On anoscopic examination the skin and mucosa are differentiated, and the use of the crypt hook and the injection treatment of internal hemorrhoids shown.

#### COMMENT

Lack of interest in and inadequate teaching of the subject of proctology leads to an underestimation of its importance in the proper management of a patient. However, this method of approach to the teaching of proctologic surgery clarifies procedures which otherwise would be

difficult to comprehend and gives one a keener understanding and a deeper appreciation of their significance. The advantages of these experimental procedures have been amply demonstrated for the past one and one-half years and are quite efficacious. It affords an opportunity of perfecting a technique for every type of proctologic operation which may well be applied to the human being. It is of inestimable value in teaching operative surgery of the anus, rectum, and colon, and when supplemented by ample clinical material makes the study of proctology considerably more interesting and profitable.

#### SUMMARY AND CONCLUSIONS

1. Laboratory experimentation of dogs and other animals has been fundamentally responsible for the many advances made in surgery in the past fifty years.

2. Training of students for the speciality of proctology has been confined entirely to apprenticeships with competent proctologists or to courses offered in a few graduate schools without the valuable aid of dog surgery.

3. The dog lends itself admirably to proctologic surgery and every conceivable type of operation may be performed with superb realism.

4. Refinements of technique, the development and solution of many intricate problems, and teaching of the art of proctologic surgery can be much enhanced by practicing dog surgery.

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# A METHOD FOR DETERMINING THE EFFICIENCY OF PREOPERATIVE SKIN STERILIZATION

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ANTISEPTICS, if considered on the basis of the role they play in the preservation of health and the frequency with which they are put to this purpose, must be awarded a prominent place in the list of therapeutic agents. Their use is not limited to the practitioner, but they are used in one form or another by individuals who are less cognizant of the deleterious effects that may be associated with their beneficial actions. It is scarcely necessary to state that antiseptics are among the most commonly misused drugs by both the lay individual and the practitioner.

In spite of the immense amount of investigation which has been done upon the action of the antiseptics since their introduction into surgery by Lister in 1865, but little is known in a quantitative way as to their ability to sterilize the intact unbroken skin. The strength of an antiseptic is standardized by determining its so-called phenol coefficient; i.e., the lowest concentration which will kill a suspension of bacteria as compared with the lowest concentration of phenol which will produce the same effect on the same culture in the same time. Occasionally the phenol coefficient is determined also in the presence of serum or other organic material, since the protein greatly alters the bactericidal power of most antiseptics. However, neither of these methods of testing bactericidal activity in vitro presents even a remote similarity to the conditions which are encountered in the attempts at preoperative sterilization of intact skin and conclusions based upon such data are therefore not applicable under these circumstances.

Due to the fact that there is no standard quantitative method to test the relative merits of skin antiseptics, a large variety of bactericidal substances and a wide range of concentrations of these substances are in use. Among those reported in the literature are potassium permanganate, bactol (cresol preparation), formalin in alcohol, chromic acid, picric acid, ammonia, cuproprotect (copper preparation), 70 per cent alcohol, essential oil of bergamot and lemon, mercuric chloride, pyxol, iodine, tincture of green soap, acriflavine, crystal violet, and brilliant green, together with an ever-growing list of relatively expensive commercial preparations. It scarcely need be mentioned that being confronted with such a wide choice is confusing to the individual who must depend on their efficient activity daily. An occasional "stitch abscess" is easily

explained by unapparent contamination, and too frequently the antiseptic is taken for granted and its efficiency remains unquestioned because of habit.

In the selection of a preoperative skin antiseptic, several points must be considered.

1. Its sterilizing efficiency should be high.
2. It should be noninjurious to the patient.
3. The time required for its action should be minimal.
4. Its cost should be low.
5. It should not damage linen or instruments.
6. It should be easy to apply.
7. It should outline the field treated.
8. It should be nonirritating to operating room personnel.
9. It should be able to continue action during and after the operation.

The results of this investigation indicate that the majority of antiseptics in common use fulfill the above requirements reasonably well, with the exception of one consideration, the cost.

Since the introduction of the iodine method of skin sterilization by Grossich in 1908, iodine has been the most commonly used skin antiseptic (Beck). Although its efficiency has been repeatedly questioned by a number of investigators (Tinker and Princee, Robb, Bonney and Browning, Decker, Turner and Catto, Bovee, Scott and Hill, Tinker and Sutton), their results can be criticized on the basis of the method used in collecting their data. In most instances, after application of the antiseptic to the skin, an area was scraped with a scalpel and the scrapings inoculated into cultural media which resulted in 55 per cent to 91 per cent sterile cultures. Skin biopsies were also taken and inoculated into broth which proved to be 40 per cent to 90 per cent sterile in various cases. However, in our experiments complete sterilization did not occur regularly with any antiseptic. Also, since the above method is not quantitative, one does not know whether the growth in broth is the result of one or many surviving bacteria. Therefore, it is difficult to draw accurate conclusions from such data. The purpose of this investigation was to determine the relative all-around efficiency of the commonly used skin antiseptics by a quantitative method that is easily carried out.

#### METHOD

The skin of the abdomen of suitable individuals, preferably those devoid of a hairy surface, was thoroughly swabbed first with benzine and then with ether to remove fatty substances. A control area was chosen, together with five or six other areas for the application of the antiseptics. Each area was then treated with a given antiseptic solution, except the control area which was treated with normal saline solution. The treatment consisted of the application of the solution by means of sterile thumb sponges in a spiral manner starting from the center and



proceeding toward the periphery until an area of about 10 cm. in diameter was treated. The solution was allowed to dry. Three such applications were made, using a new thumb sponge for each application. When the last coat became dry, the antiseptic was removed with three applications of Richardson's solution. Culture plates were then applied, agar surface downward, taped to the skin and allowed to remain in position for fifteen minutes, after which time they were removed and placed into sterile Petri plates. Colonies were counted after twenty-four hours' incubation at 37° C. Any sterile plates were inoculated with known staphylococci from the skin and reincubated to eliminate the possibility of an existing bacteriostatic effect due to absorption of antiseptic by the agar from the skin surface.



Fig. 1.—Impression plates in position on patient's abdomen.

The culture plates were prepared as follows: Ordinary 10 per cent blood-nutrient agar was prepared and poured into watch glasses having a diameter of 6 cm. which had been previously placed within Petri plates and sterilized. The watch glasses were filled level full and the agar was allowed to solidify overnight in a refrigerator. Watch glasses were used since they required a smaller amount of medium to fill them (10 to 15 c.c.), and they were more convenient to tape into position than ordinary Petri plates. Also they were of a convenient size, allowing them to be placed within the ordinary Petri plates for the period of incubation.

## RESULTS

The results are tabulated in the accompanying tables. As will be noted, the most common organisms on the skin are staphylococci and diphtheroids. Occasionally an aerobic sporeformer or a *Pseudomonas pyocyaneus* was encountered, but since neither of these is very significant as a pathogen, and since they occurred so rarely and then only on control plates, they were not recorded. The staphylococci and diphtheroids, however, since they are so common on the skin and are usually found in infected wounds, must be considered in any method purposing to destroy them.

None of the antiseptics used was able regularly to sterilize the skin completely. Our results do not agree with those of Tinker and Sutton, who state that superficial layers of skin are frequently sterile in normal clean individuals as determined by culturing scrapings of the superficial epithelium. In the 71 control areas in our series, there occurred an average of 342 colonies on each blood agar impression plate or about 12 colonies per square centimeter of skin. These control plates were taken from any one of four areas: the breast, the epigastric region, the umbilical region, or the hypogastric region. On a number of occasions impression plates were taken on all four areas simultaneously and showed a closely corresponding number of colonies developing on the plates.

A rather surprising result is the fact that the solvent (50 per cent alcohol, 10 per cent acetone) is itself highly germicidal and is able to destroy more than 96 per cent of the organisms present on the skin. This solvent was used to dissolve the antiseptic substances used in these experiments, since Vaichulis and Arnold showed that these concentrations had the best antiseptic value in the test tube and a good defatting action on the fatty substances in the skin. It also dries readily, yet not too rapidly to prevent adequate antiseptic action. It has a low surface tension and is thus more able to reach the tiny depressions in the skin surface.

The addition of any of the antiseptics used to the alcohol-acetone solvent served only to destroy an additional 2 per cent to 3 per cent of the organisms. Tincture of green soap is by far the poorest of the substances tested to use for destroying either staphylococci or diphtheroids. In one case more organisms were present on the treated side than on the control, which can be explained on the ability of soap to break up large aggregates of bacteria into smaller clumps or single cells, each giving rise to a single colony; therefore, the more aggregates, the more colonies.

One per cent iodine is shown to be very efficient as a skin antiseptic, but it does not prove practical, since very irritating vapors (probably an iodoacetone) arising as the solution evaporates from the skin make it almost impossible to use it. It has a further drawback in that it must be removed from the skin with alcohol or Richardson's solution to pre-

TABLE

	MERCRESIN (COMMERCIAL)		IODINE 1%		HgCl <sub>2</sub> 1-1500 TRICRESOL ½%		TRICRESOL 2%		METAPHEN (COMMERCIAL)	
Control	420s	120d	420s	110d	53s	12d	420s	110d	420s	110d
Antiseptic	0s	0d	1s	0d	2s	0d	0s	0d	0s	0d
Control	300s	180d	300s	180d	66s	18d	300s	180d	300s	180d
Antiseptic	1s	2d	8s	0d	0s	0d	2s	0d	6s	0d
Control	120s	14d	80s	60d	53s	12d	1,200s	300d	1,200s	300d
Antiseptic	0s	1d	0s	0d	0s	0d	0s	0d	0s	0d
Control	1,200s	300d	1,200s	300d	600s	30d	300s	140d	300s	140d
Antiseptic	1s	0d	1s	0d	1s	0d	2s	0d	5s	0d
Control	300s	140d	300s	140d	66s	18d	1,100s	80d	380s	140d
Antiseptic	1s	0d	1s	0d	2s	0d	13s	0d	3s	1d
Control	120s	26d	500s	180d	600s	30d	210s	36d	120s	14d
Antiseptic	0s	0d	10s	0d	1s	0d	2s	0d	1s	0d
Total for controls	2,460s	780d	2,800s	970d	1,440s	120d	3,530s	856d	2,720s	884d
Total for antiseptics	3s	3d	21s	0d	6s	0d	19s	0d	15s	1d

\*S = staphylococci; d = diphtheroids.

vent iodine burns. This is a definite disadvantage since, with its removal, antiseptic action ceases and the bacteria in the sweat glands that are brought to the surface when vasodilation takes place during the operation remain viable and the wound is thus liable to infection. How serious this is has not been shown experimentally, but such results as those reported by Meleney, in which he states that 12½ per cent of wounds had some inflammatory reaction, many of which were probably infectious in nature, may well be explained by this possible source of wound contamination.

Among the least expensive substances used, 0.1 per cent mercuric chloride in alcohol-acetone or a solution of 2 per cent trieresol in the same solvent proved to have a high bactericidal action. However, diphtheroids are not always killed by mercuric chloride, and 2 per cent trieresol occasionally produces a slight erythema in more sensitive individuals. Trieresol, nevertheless, does kill diphtheroids. Since the amount of either substance added to one gallon of solvent costs less than three cents, it was decided to try a combination of the two substances in somewhat lesser concentrations. A combination of 1:1,500 mercuric chloride and ½ per cent trieresol in alcohol-acetone solution proved to be efficient in destroying 99.6 per cent of the staphylococci and 100 per cent of the diphtheroids. A small amount of acid fuchsin or eosin Y or a combination of both may be added to the antiseptic solution to outline the field to which the antiseptic is applied. This was not done in the initial experiments, as we wanted to detect any erythema or skin irrita-

I\*

IODINE 1% TRICRESOL ¾%		HgCl <sub>2</sub> 1-1000		IODINE 1% TRICRESOL ¾% IN 70% ALCOHOL		HARRING- TON'S SOLUTION		MERTHIO- LATE (COMMER- CIAL)		ALCOHOL 50% ACETONE 10%		TINCTURE GREEN SOAP	
53s	12d	80s	60d	600s	30d	500s	180d	420s	110d	53s	12d	500s	180d
0s	0d	4s	2d	6s	0d	2s	0d	0s	0d	4s	0d	80s	70d
66s	18d	80s	60d	600s	30d	380s	140d	300s	180d	53s	12d	380s	140d
2s	0d	2s	0d	2s	0d	0s	0d	8s	0d	6s	0d	500s	190d
53s	12d	1,200s	300d	110s	14d	120s	26d	1,200s	300d	420s	110d	120s	26d
0s	0d	2s	0d	2s	0d	1s	0d	1s	0d	0s	1d	36s	8d
66s	18d	300s	140d	110s	14d	120s	14d	300s	140d	300s	180d	120s	14d
1s	0d	0s	1d	4s	0d	24s	0d	0s	4d	16s	8d	96s	8d
600s	45d	1,100s	80d	110s	14d	1,100s	80d	380s	140d	80s	60d	1,100s	80d
1s	0d	18s	0d	2s	0d	16s	0d	30s	22d	3s	0d	220s	80d
110s	14d	210s	36d			210s	36d	120s	26d	500s	180d	210s	36d
1s	0d	0s	0d			3s	0d	1s	0d	22s	8d	40s	18d
952s	119d	2,970s	676d	1,530s	102d	2,430s	476d	2,720s	896d	1,406s	554d	2,430s	476d
5s	0d	26s	3d	16s	0d	46s	0d	40s	26d	51s	17d	982s	374d

tion that might occur, but neither was noted when these concentrations were used. The following formula is used for preparing the solution:

Alcohol, 95 per cent	525 c.c.
Acetone	100 c.c.
Water	375 c.c.
Tricresol	5 c.c.
Mercuric chloride	0.7 gm.
Eosin Y	0.6 gm.
Acid fuchsin	0.08 gm.

Since this mercuric chloride-tricresol combination in alcohol acetone fulfills the requirements set up for a skin antiseptic and since the cost of the preparation is astoundingly minimal as compared to commercial preparations having similar properties, its use for skin sterilization is

TABLE II

ANTISEPTIC	% STAPHYLOCOCCI REDUCED	% DIPHTHEROIDS REDUCED	% TOTAL REDUCTION
Mereresin (commercial)	99.88	99.62	99.82
Iodine 1%	99.53	100.00	99.65
Tricresol 0.5%			
HgCl <sub>2</sub> 1-1500	99.60	100.00	99.62
Tricresol 2%	99.47	100.00	99.57
Metaphen (commercial)	99.45	99.89	99.56
Iodine 1%			
Tricresol ¾%	99.48	100.00	99.54
HgCl <sub>2</sub> 1-1000	99.13	99.56	99.21
Iodine 1% Tricresol			
0.75% in 70% alcohol	98.96	100.00	99.02
Harrington's solution	98.11	100.00	98.42
Merthiolate (commercial)	98.53	97.10	98.18
Alcohol 50% Acetone 10%	96.38	96.94	96.53
Tincture green soap	59.59	21.43	53.64

highly recommended. In actual use in preoperative sterilization of the skin, it has proved to be an efficient and convenient preparation.\*

### CONCLUSIONS

1. A simple method for the determination of the efficiency of skin antiseptics is described.
2. An average of twelve staphylococci and diphtheroids per square centimeter was found to be present on normal cleanly skin.
3. The applications of 50 per cent alcohol, 10 per cent acetone solution, a common solvent for antiseptics, destroy 96 per cent of the bacteria on the skin.
4. Only 2 per cent to 3 per cent more of the skin organisms are killed when any commonly used skin antiseptic is added to this solvent.
5. Tincture of green soap alone is very inefficient in skin sterilization, killing only 53 per cent of the bacteria on the skin.
6. A concentration of 0.07 per cent mercuric chloride and 0.5 per cent tricresol (costing about 5 cents per gallon) in 50 per cent alcohol, 10 per cent acetone solution is an efficient, inexpensive skin antiseptic.

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\*This solution has been used in all types of general surgery at the University of Minnesota Hospitals for the past four months.

# A CLINICAL CLASSIFICATION OF CANCER OF THE BREAST

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THE need of a standard clinical classification for cases of mammary cancer becomes evident when one reviews recent statistics of the treatment and end results in this malady. It becomes at once apparent that the published reports appear hopelessly conflicting and, at times, misleading, mainly due to the fact that the tabulated results of treatment fail to describe accurately the degree of involvement when therapy is initiated. In other words, the efficacy of the indicated form of treatment in an advanced stage of the disease is not comparable with the results obtained in the early stages when the lesion is confined to the breast itself. For example, some surgical clinics report that radical surgery alone gives five-year cures in from 60 to 70 per cent of their cases; whereas, other groups report that only 30 to 40 per cent of their patients are well and free from disease five years after radical mastectomy. Although the technique of radical surgery for breast carcinoma differs very slightly in various clinics, yet this discrepancy in statistical reports exists and is probably due to the marked difference in the criteria of operability among surgeons. What one surgeon would consider an operable case, another would hold inoperable. In other words, there is as yet no uniformity in the classification of these patients. Hence, until this is accomplished, there can be no agreement upon the proper course to pursue that would offer the most favorable outcome, and, by the same token, there can be no trustworthy statistical analysis of the end results of treatment.

Therefore, until all cases can be made to fit into a clinical classification that is practical and is universally accepted, there can be only confusion and uncertainty preventing further progress in the management of this disease.

Many years ago, Steintal<sup>1</sup> presented a classification, based on clinical observation, which lacks clarity and, therefore, is impractical. More recently, Portmann<sup>2</sup> and Pfahler<sup>3</sup> have classified breast tumors into three clinical groups, but, here again, the divisions are not entirely clear cut and accurate and many cases fail to fit into any of their groups. The classification of mammary cancer into clinical stages is not to be confused with the grading of these tumors (MacCarty)<sup>4</sup> into four divisions which represent the microscopic appearance of the predominant malignant cell in the sections. These types range from the adult or well-differentiated cells (Grade 1) to the anaplastic, immature, or embryonal cells (Grade 4), with the other two divisions representing intermediate forms.

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The classification to be presented is not based on pathologic or microscopic material, but is entirely predicated on clinical evidence evolved from physical examination, particularly inspection and palpation.

Each patient with the diagnosis of mammary cancer should be properly classified according to the stage of her disease at the time she first presents herself for treatment. The clinical classification of patients with breast cancer given in Table I is therefore suggested.

TABLE I  
CLASSIFICATION OF BREAST CANCER

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STAGE 1

*Primary tumor*

3 cm. or less in diameter

*Skin*

Not adherent to tumor

*Underlying tissues*

Growth not adherent to pectoral muscle or fascia

*Axilla*

No palpable nodes

*Supraclavicular fossa*

No palpable nodes

*Opposite breast and regional lymph nodes*

Negative

*Distant metastasis*

None

STAGE 2

*Primary tumor*

More than 3 cm. and less than 6 cm. in diameter

*Skin*

Not adherent to growth

*Underlying tissues*

Not adherent

*Axilla*

One to three small nodes palpable, the largest not more than 2 cm. in diameter

Nodes freely movable

*Supraclavicular fossa*

No palpable nodes

*Opposite breast and regional lymph nodes*

Negative

*Distant metastasis*

None

STAGE 3

*Primary tumor*

Larger than 6 cm. in diameter

*Skin*

Partially or completely adherent to tumor

Skin edematous

Skin inflamed (inflammatory cancer)

Skin ulcerated

*Underlying tissues*

Tumor partially or completely fixed

*Axilla*

More than 3 nodes palpable

One or more nodes larger than 2 cm. in diameter, regardless of the number palpable

One or more nodes adherent or fixed

One or more nodes ulcerated

Lymphedema of the upper extremity of the affected side (in the absence of radical mastectomy)

*Supraclavicular fossa*

One or more nodes palpable

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TABLE 1—CONT'D

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*Opposite breast and regional lymph nodes*

- Intramammary tumor
- Subcutaneous mass
- Cutaneous nodule
- Palpable node in contralateral axilla and/or supraclavicular fossa

*Distant metastasis*

- To the rib or ribs
- To the pleura
- To the mediastinum
- To the lung
- To the spine and/or bones

## STAGE 4 (POSTOPERATIVE)

*Local recurrence*

- In the skin, scar, stitch holes
- In the subcutaneous tissues
- In the residual breast tissue (incomplete operation)

*Regional recurrence*

- In the axilla
- In the supraclavicular fossa

*Opposite breast and regional lymph nodes*

- In the mammary gland
- In the skin
- In the axilla
- In the supraclavicular fossa

*Distant metastasis*

- To the chest
  - To the skeletal system
- 

Stage 1 carcinomas need very little explanation. Freely movable tumors measuring 3 cm. or less in diameter with no palpable evidence of nodes in the regional lymph-bearing areas belong to this group. In Stage 2 the primary tumor is larger but measures less than 6 cm. in diameter and is not particularly adherent to the overlying skin or underlying pectoral muscle. Even without enlargement of the regional lymph nodes and without metastasis or contralateral involvement, such growths belong to this group. If one to three axillary nodes are palpable, each measuring less than 2 cm. in diameter, the patient is still relegated to Stage 2. Even with a small, freely movable tumor in the breast (3 cm. or less in diameter), but with one to three small palpable nodes in the axillary fossa, the case belongs to Stage 2.

If more than three nodes are felt in the axilla, or if at least one palpable node measures more than 2 cm. in diameter or is definitely fixed or ulcerated, or if a node is palpable in the supraclavicular fossa, the case is classified in Stage 3. Regardless of the other findings, a patient in Stage 3 presents either a large primary tumor measuring over 6 cm. in diameter or a small mass which is adherent to the skin or to the underlying tissues or both. Evidence of distant metastasis or involvement of the contralateral breast or nodes immediately places the case in Stage 3.

When the cancerous breast is edematous, the case is placed in Stage 3, regardless of the other findings. Similarly, when the skin is inflamed, the so-called inflammatory cancer, the lesion is classified in Stage 3.



Cancer *en cuirasse* and nodular or ulcerated involvement of the skin from the primary growth or a regional node belong to the same stage. An adherent or fixed cancer of the breast, regardless of the other factors, is similarly classified. When the upper extremity of the affected side reveals an edematous appearance in the absence of radical surgery, the local lesion is assumed to have spread to the lymphatics draining this region. With block of the lymph channels with malignant cells resulting in lymphedema, the case is considered advanced and properly belongs to Stage 3. This may occur, however, without pronounced involvement of the axillary lymph nodes.

Thus, it is seen that it is not at all necessary for each case to present all of the positive findings described in each stage, but, on the contrary, any one positive characteristic relegates the lesion to the corresponding group.

Stage 4 classifies only those patients with involvement after mastectomy. The recurrence may be, locally, in the anterior chest wall of the operated side; regionally, in the lymph nodes; distantly, in the chest or osseous system, or by extension to the contralateral breast and glands. The *modus operandi* of the latter involvement is by way of the internal mammary lymphatics and parasternal glands to the mediastinum and then by back pressure through the same route on the opposite side to the contralateral breast.

#### SUGGESTIONS AND CONSIDERATIONS

Every case of suspected breast carcinoma should have a biopsy of the primary growth. It is immaterial whether this is performed by scalpel, cautery, aspiration, punch, or needle as long as a satisfactory specimen is obtained and treatment is immediately instituted. If a tumor is elicited in each breast, both lesions should be biopsied. A roentgenogram of the chest is recommended in all cases, even when no extension to the lungs or mediastinum is suspected. This study is valuable evidence for comparison with films that may be necessary at some subsequent date in order to determine the presence or absence of extension into the chest. Any part of the body faintly suspicious of metastasis requires an immediate roentgen examination. The skeletal system is particularly susceptible to metastatic involvement.

Although the requisites for each stage of the disease are clearly stated, there are occasions when a case may require reclassification. An instance of such a change is when a patient clinically classified in Stage 1 (a small, freely movable breast tumor without palpable axillary nodes) at the initial examination turns out to have malignantly invaded nodes in the axilla at the operating table (Stage 2).

#### TREATMENT

The clinical classification above described is not only of value in the compilation of accurate statistics, but is essentially of major importance

in the management and prognosis of the case. The classification of cases of carcinoma of the cervix uteri by Schmitz<sup>5</sup> has proved particularly valuable in prognosis rather than in therapy because these cases are radiologic problems. However, in breast cancers the management is different. Surgery and irradiation are the two forces usually combined to attack the disease for the best ultimate result. Hence, the four stages of the disease indicate not only the probable outcome but also the proper plan of treatment.

We believe that cases that fit into Stages 1 and 2 require radical surgery and intensive irradiation. Preferably, the roentgen treatments should be administered preoperatively and postoperatively, especially in Stage 2. Statistics from many well-accredited clinics show that survival rates in these patients increase from 30 to 40 per cent when radical surgery alone is performed to from 50 to 60 per cent when surgery is combined with irradiation. Cases falling into Stages 3 and 4 are essentially radiation problems with or without occasional conservative surgery, if needed. In these stages the roentgen rays or radium or both are used. In Stage 3 only from 5 to 10 per cent are salvaged; in Stage 4, even less. In these stages the local disease has already become disseminated. The futility of radical surgery in these advanced cases is readily comprehended. Yet radiation therapy will usually prolong their lives, reduce pain and suffering, and change an intolerable existence to a relatively comfortable life.

#### SUMMARY

A clinical classification of all mammary cancers into four stages is presented. The exact requirements for each group are indicated. This classification appears simple, rational, and practical. To us it has already been of inestimable service in more than 200 cases. Such a classification is extremely valuable in simplifying statistical reports of five-year cures, analyzed in the four standardized clinical stages of the disease, and in outlining the proper plan of treatment and in prognosticating the final outcome for each division. We believe that patients in Stage 1 and Stage 2 should be treated by radical surgery and intensive (radical) irradiation. Those falling in Stages 3 and 4 require x-rays or radium therapy or both, with or without conservative surgery, if and when required.

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#### TREATMENT

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There were a few strands of tissue in the region of the bifurcation of the carotid which were connected with the tumor and which, in retrospect, may have represented nerve fibers. No vessels of any consequence entered the tumor. It was readily enucleated without injury to the adjacent structures. The wound was closed in layers with fine silk.

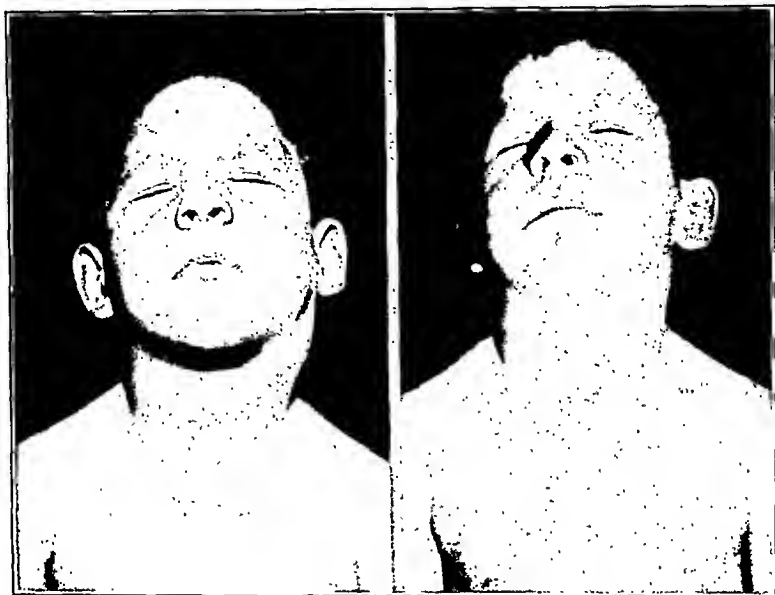


Fig. 1.—Preoperative (A) and postoperative (B) views of patient.

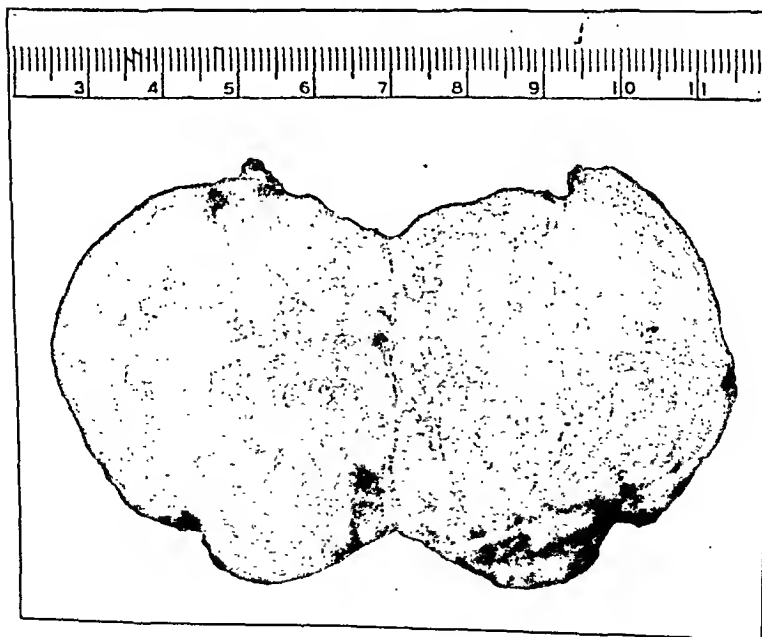


Fig. 2.—Gross specimen.

# CERVICAL SYMPATHETIC GANGLIONEUROMA

## CASE REPORT AND REVIEW OF THE LITERATURE

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**C**ERVICAL sympathetic ganglioneuroma is one of the rarest of neck tumors. The present case, which is the only one in the records of the New Haven Hospital, is added to the thirteen previously reported, and the literature is reviewed.

### CASE REPORT

J. C., aged 5 years, white, male, was admitted to the New Haven Hospital July 15, 1937, complaining of a mass in the left side of the neck which had been present since he was 1 year old and which had grown slowly.

When the tumor was first noticed, he had been brought to the Out-Patient Department where a diagnosis of acute tonsillitis and acute bilateral cervical adenitis was made. Swellings were described at both angles of the jaw, the right larger than the left and not tender; the left, firm and sensitive. Subsequently a right submaxillary abscess was drained. The wound healed promptly. In May, 1936, he was again seen because of the persistent mass in the left neck. He had had, during the preceding three years, frequent colds, a chronic cough, and nasal discharge and had always talked with a peculiar hoarseness. The tonsils were enlarged, the pillars injected. The mass in the neck was described as a moderately soft, nonfluctuant, freely movable tumor about 4 cm. in diameter below the angle of the jaw, below which were several nontender lymph nodes. The tuberculin test was negative to 1/10 mg. Tonsillectomy and adenoidectomy were performed. Direct laryngoscopy revealed nothing abnormal. The swelling and hoarseness persisted. Family history and past history were not significant.

*Examination.*—There was a noticeable hoarseness and a tendency to mouth breathing. There were no observed eye signs and no evidence of sympathetic disturbance. Extending downward from just below the lobe of the left ear along the anterior border of the sternocleidomastoid muscle was a solid, ovoid mass measuring 6 by 4 cm., over the surface of which the external carotid was seen and felt. The remainder of the examination was essentially normal. The blood Kahn test was negative; the urine and blood examinations, normal. A chest film showed slight pleural thickening on the right. The preoperative diagnosis was that of a carotid body tumor.

*Operation.*—July 16, 1937: An incision about 6 cm. in length was made along the anterior border of the sternocleidomastoid, and the deep cervical fascia divided along the edge of the muscle, bringing into view an enlarged lymph node overlying a deeper tumor mass. The node was removed. The tumor was firm, well encapsulated, avascular, and pale. It had displaced the internal jugular vein posteriorly. The external carotid artery lay over the anterior portion of the mass, and the internal carotid posterior to it. The hypoglossal nerve ran across the tumor.

tion (Fig. 5). Many of these strands show balloon-like dilatations which resemble those found in degenerated myelin nerve sheaths.

Scattered diffusely throughout the sections are a few small aggregations of small round cells. They have a very thin rim of pale eosinophilic cytoplasm and round deeply staining basophilic nuclei.

The tumor is fairly well supplied with thin-walled small patent blood vessels. No mitotic figures are seen and no multinucleated ganglion cells.

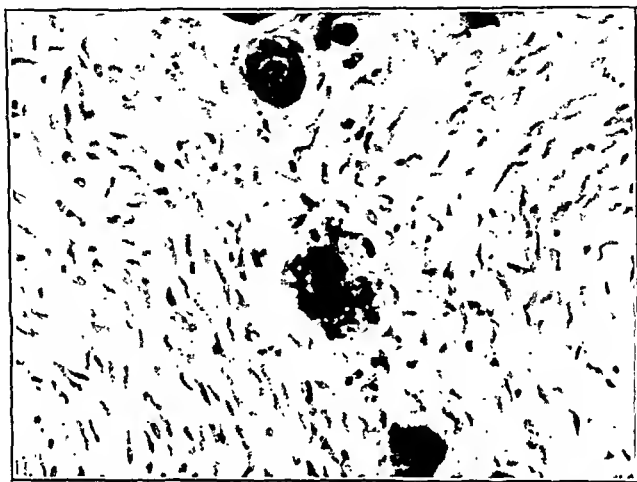


Fig. 4.—Photomicrograph showing Nissl bodies in ganglion cell (toluidin blue,  $\times 250$ ).

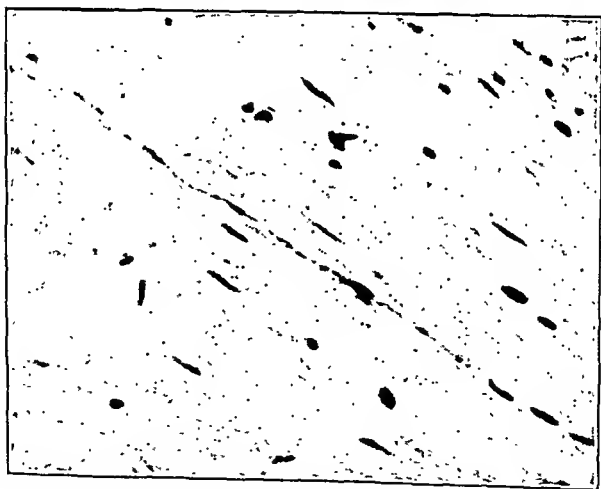


Fig. 5.—Photomicrograph showing a strand of myelin with balloon-like dilatations (Pal-Weigert,  $\times 250$ ).

#### REVIEW OF THE LITERATURE

In McFarland and Sappington's review,<sup>1</sup> 17 of the 127 cases of ganglioneuroma are said to have been situated in the cervical region. We have been able, however, to find only 13 cases definitely arising from cervical

The postoperative course was entirely uneventful except for the appearance of a Horner's syndrome on the left, with myosis, ptosis, and enophthalmos. No alteration in sweating was noted.

No change has occurred during the past eleven months except that the enophthalmos and ptosis are perhaps less marked. The hoarseness has not altered.

*Gross Pathology.*—The specimen is a well-encapsulated mass of tissue which measures 6 by 4.5 by 3 cm. (Fig. 2). Its external surface is of a uniformly pink-yellow color and smooth except for a few tags of fibrous tissue. The tumor is of a rubbery consistency and cuts easily. The dull yellow-white cut surface is slightly irregular and is formed by whorls and strands of what appears to be fibrous tissue. The capsule is thin, dense, and homogeneous and is pink-yellow in color. Sections of the tissue are fixed in 10 per cent neutral formolin, imbedded in paraffin and in celloidin, and stained with hematoxylin and eosin, Masson polychrome stain, Pal-Weigert myelin sheath stain and toluidin blue Nissl-body stain.

*Microscopic.*—The tumor has a well-defined capsule of dense fibrous tissue (Fig. 3). The stroma is formed by bundles of delicate fibers which are more compact in the periphery than in the center. There are many slender spindle cells in all areas. In the hematoxylin and eosin preparation their cytoplasm takes a pale pink stain and their long oval nuclei a deep basophilic stain.

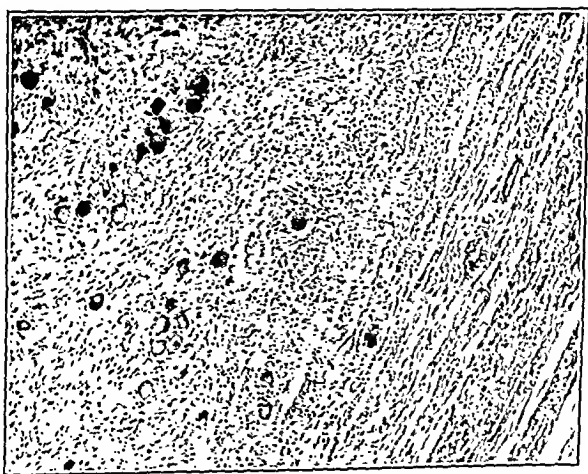


Fig. 3.—Photomicrograph showing the capsule, the groups of ganglion cells, and the fibrous stroma (hematoxylin and eosin,  $\times 60$ ).

The most prominent feature of the tumor is the ganglion cells. They are arranged in clumps in certain areas and are scattered diffusely in other portions (Fig. 3). Most of them have homogeneous eosinophilic cytoplasm and eccentrically placed pink oval nuclei with prominent nucleoli. Others have foamy, pale basophilic cytoplasm either with no visible nuclei or with nuclei which are granular, vacuolated, or have a prominent, very delicate chromatin network. The toluidin blue stain demonstrates the presence of small granular dark bodies in the cytoplasm of the cells, particularly in the peripheral zones (Fig. 4). A rare ganglion cell is unipolar, and no bipolar or multipolar ones are seen. Many have a capsule of a single layer of very flat cells.

In the Masson polychrome stain most of the fibers are light green, but a few however, are pink. An occasional myelinated fiber is seen in the Pal-Weigert prepara-

## I.

## SYMPATHETIC GANGLIONEUROMA

CAROTID ARTERY	OPERATION	AUTOPSY	HORNER'S	CLINICAL IMPRESSION	PATHOLOGY	REMARKS
----	Difficult Incomplete	0	Preoperative narrowing of lid slit; postoperative ptosis	----	Ganglion cells, nerve fibers and connective tissue	
----	----	+	----	----	Ganglion cells, some multinucleated	
Anterior	Easy	0	Preoperative enophthalmos	----	Ganglion cells, sheath of Schwann cells, nonmyelinated and few myelinated fibers	
Lateral, superficial	0	+	----	Tuberculous adenitis	Ganglion cells, a few multinucleated; nonmyelinated nerve fibers	
Anterior	Easy	0	Present 4 days postoperatively; ptosis, myosis, and anhydrosis	----	Ganglion cells, chiefly apolar; nerve fibers, very few myelinated	
----	+	0	Ptosis, pupillary change	"Gland"	Ganglion cells	
Anterior and superficial	+	0	----	Branchiogenic cyst or tuberculous	Ganglion cells, nerve fibers, round cells	
Common and both branches superficial	Easy	0	Slight paresis right face; ptosis, dilatation right pupil for 3 to 4 years	Tuberculous adenitis	Ganglion cells, small round cells; good vascular supply; no mitoses	Said to have increased in size with throat infection and to have decreased in free intervals; adenoidectomy, 18 mo.; tonsillectomy, 2 yr.
----	+	0	----	----	Ganglion cells, fibrous	
Superficial	Easy	0	Ptosis, myosis, enophthalmos	----	"Typical ganglioneuroma,"	Cervical sympathetic divided at operation; anastomosis impossible



TABLE

CASE REPORTS OF CERVICAL

AUTHOR	AGE	SEX	SIDE INVOLVED	ONSET AGE	GROWTH	CHARACTER	SIZE	TRACHEAL DISPLACEMENT	JUGULAR VEIN
DeQuervain <sup>11</sup> (1899)	13 yr.	F	L	7	Slow	Smooth, hard	Small fist	----	----
Benda <sup>12</sup> (1904)	Child	--	R	--	--	----	--	----	----
Glinski <sup>13</sup> (1906)	10 yr.	F	L	7 mo.	Slow progressive	Firm, irregular, slightly movable	9 by 6½ by 3½ cm.	3 cm. to right	----
Woods <sup>14</sup> (1906)	32 yr.	M	R	--	--	Firm, encapsulated	9 by 8 by 4 cm. 180 gm.	----	Lateral superficial
Freund <sup>15</sup> (1913)	5¾ yr.	M	R	4¾	Rapid in recent months	Firm, coarsely nodular	9 by 6 by 4 cm.	To left	Posterior
Sommerfelt <sup>16</sup> (1920)	36 yr.	F	L	30	Slow	Firm, slightly nodular	Goose egg	----	----
Geymüller <sup>17</sup> (1919)	5 yr.	M	L	Few weeks	Slow	Firm	6 by 4 by 3 cm.	----	Superficial
Stout <sup>18</sup> (1924)	2½ yr.	F	R	5 wk.	--	Soft, irregular	7 by 4 by 3½ cm.	----	Posterior
Harbitz <sup>19</sup> (1926)	22 yr.	F	--	2	--	Elastic, resilient, fibrous	13 by 8 cm.	----	----
MacAuley <sup>20</sup> (1930)	6 yr.	M	L	Few days	Slow	Firm, encapsulated, "fibroid"	Tangerine	----	Posterior

## I—CONT'D

CAROTID ARTERY	OPERATION	AUTOPSY	HORNER'S	CLINICAL IMPRESSION	PATHOLOGY	REMARKS
----	+	0	----	----	Ganglion cells, small less well-differentiated cells; non-myelinated nerve fibers	Also had right retroperitoneal tumor histologically identical with neck tumor
----	+	-	----	----	No details given	
----	+	+	----	----	No details given	
External carotid anterior and superficial	+	0	Ptoſis, myosis, enophthalmos	Carotid body tumor	See text	

One patient had a second retroperitoneal ganglioneuroma. The sympathetic trunk was rarely identified at operation.

## DISCUSSION

We are unaware of any instance in which a cervical sympathetic ganglioneuroma has been diagnosed preoperatively. Though an exceedingly rare tumor, the need for preoperative diagnosis is obvious. This is especially true because of the relatively high incidence of Horner's syndrome, a rather distressing sequela which must necessarily follow in a certain number of cases and which is usually avoidable in the removal of other benign neck tumors.

Certain features are present with sufficient regularity to be very suggestive although there are no pathognomonic signs or symptoms. The usual complaint is simply a swelling in the neck, ordinarily painless, slow in growth, and of long duration, generally dating back to early childhood. Rarely there is respiratory distress and tracheal compression. The apparent, though probably unreal, fluctuation in size occasionally has led to a diagnosis of cervical adenitis for which tonsillectomy has been performed. The tumors are firm, encapsulated, with freely movable skin over them and with relative fixation to the deeper structures. Of especial aid in the differential diagnosis is the displacement of the great vessels. The internal jugular vein lies posterior to the tumor and is generally not visible, but the carotid artery lies superficial to the mass and is readily seen pulsating over it. In rare instances sympathetic disturbances, such as ptosis and enophthalmos, may be found.

The treatment is excision, a procedure which is generally not difficult.

Other reporters<sup>22</sup> have dealt extensively with the pathology. Nerve tumors may show any stage of differentiation from the primordial cell to

TABLE

AUTHOR	AGE	SEX	SIDE INVOLVED	ONSET AGE	GROWTH	CHARACTER	SIZE	TRACHEAL DISPLACEMENT	JUGULAR VEIN
Haven and Weil <sup>21</sup> (1932)	23 yr.	F	L	14	Slow	----	Child's fist	----	----
Lewis and Geschickter <sup>10</sup> (1934)	10 yr.	M	--	9	--	----	--	----	----
	4 yr.	M	--	1	--	----	--	----	----
Shumacker and Lawrence (1938)	5 yr.	M	L	1	Slow	Firm, encapsulated	6 by 4.5 by 3 cm.	None	Posterior

ganglia with the typical histologic picture. The available data on these are presented in Table I. Excluded are certain ones mentioned by others as cervical tumors which actually either arose definitely in the mediastinum or which involved both neck and mediastinum in such a manner as to make the point of origin uncertain.<sup>2-5</sup> Also omitted are certain others in which the tumor as described was probably a neuroblastoma, a sympathicoblastoma, or mixed in type.<sup>1, 6-11</sup>

The patients ranged in age from 2½ to 36 years. Seventy per cent of the tumors were in children. In many the tumor had been noted from infancy or early childhood. The sexes were equally affected. Seven of the eleven cases with available data arose on the left side. In almost all the growth had been slow. The tumor was generally described as firm, fairly smooth, and well encapsulated. The size varied from 6 by 4 by 3 cm. to 13 by 8 cm. In a few there were respiratory embarrassment and tracheal deviation. Ordinarily the jugular vein lay posterior to the mass and the carotid artery superficial to it. In 12 cases an operation was performed; in 2 the diagnosis was made post mortem; and in 1, removed at operation, autopsy was subsequently performed. In 4 cases a typical Horner's syndrome developed postoperatively; in 1 there was slight facial paresis, ptosis, and dilatation of the pupil on the affected side; in 1, enophthalmos was noted preoperatively; and in 1, with a definite postoperative ptosis, slight narrowing of the lid slit had been observed before operation. The clinical diagnosis was most often that of tuberculous adenitis. Other preoperative diagnoses were "gland," branchial cleft cyst, and carotid body tumor. Pathologically they all showed a picture quite similar to that described in our case. In one instance the author suspected that the tumor might have arisen from the vagal ganglion.

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16. Sommerfelt, L.: Ein Fall von Ganglioneurom am Hals, Zentralbl. f. allg. Pathol. u. path. Anat. 30: 641-656, 1920.
17. Geymüller, E.: Beiträge zur Kenntnis der Ganglioneurome und ihrer Beziehungen zu der Recklinghausen'schen Krankheit, Beitr. z. klin. Chir. 115: 712-722, 1919.
18. Stout, A. P.: Ganglioneuroma of the Cervical and Thoracic Sympathetic Ganglions, J. A. M. A. 82: 1770-1774, 1924.
19. Harbitz, F.: Ganglioneuroma in Sympathetic Nerve in Neck; Suprarenals in Addison's Disease, Norsk. Mag. f. Lægevidensk. 87: 371-376, 1926.
20. MacAuley, H. F.: Ganglioneuroma of the Cervical Sympathetic, Irish J. M. Sc. 55: 297-300, 1930.
21. Haven, H., and Weil, A.: Multiple Ganglioneuroma, Arch. Path. 13: 713-715, 1932.
22. Wahl, H. R.: Neuroblastomata, J. Med. Research 30: 205-260, 1914.

the mature ganglion cell. They may be composed entirely of neuroblasts or of a combination of neuroblasts, sympathieoblasts, and ganglion cells and in these instances are malignant. If, however, they are formed by mature ganglion cells and nerve fibers as in our tumor, they are, as far as is known, perfectly benign. It is our feeling that the term ganglioneuroma should be applied exclusively to the tumors showing ganglion cells and nerve fibers without sympathieoblasts or neuroblasts.

#### SUMMARY

1. A case of cervical sympathetic ganglioneuroma is added to the 13 previous reports appearing in the literature.

2. These tumors appear in children or young adults. They are slowly growing, firm, and fairly smooth. Tracheal displacement and respiratory embarrassment are rare. Usually the carotid artery is either visible or palpable anterior to the tumor. Sympathetic disturbances, such as ptosis, myosis, and enophthalmos, are common postoperatively but may also be present preoperatively.

3. Pathologically they are characterized by a fibrous tissue stroma supporting clumps of ganglion cells and strands of nerve fibers which are usually nonmyelinated.

4. In no known instance has the correct diagnosis been made preoperatively.

We wish to extend our thanks to Dr. Robert Tennant for his advice in helping us prepare this report.

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## SIMILAR GOITERS IN MONOZYGOTIC TWINS

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(From the Mayo Foundation)

THE role of heredity in susceptibility to disease has not been definitely determined. In discussing the etiologic factors of any disease, the cause of which is not entirely clear, medical men usually mention the possibility of a hereditary factor. Probably since the earliest times physicians have asked their patients about the diseases to which their forebears and relatives have fallen victims, without being able to evaluate the information thus obtained, but suspecting that it would be of value if only the key were known. For many years writers and investigators have interested themselves in the study of twins with the hope that new hereditary factors could be discovered and properly evaluated. Recently Freeman said that twins are the best subjects of study to determine the influence of heredity and environment. In 1883 Sir Francis Galton wrote: "Twins have a special claim upon our attention; it is that their history affords us a means of distinguishing between the effects of tendencies received at birth and those that were imposed by the special circumstances of their after lives."

Dizygotic twins are those which result from the simultaneous fertilization of two ova by two spermatozoa. They are no more alike than are brothers and sisters who are not twins, and may be of the same or opposite sex. Their simultaneous conception is a coincidence and, strictly speaking, they are not true twins. Newman has said that "twinning is twain-ing or two-ing, the division of an individual or an organ into two equivalent and more or less completely separate individuals or organs." Identical or homologous twins are always monozygotic, are necessarily of the same sex and are nourished by one placenta which has two cords, two amnions, and a single chorion. It is solely with identical twins that we are concerned in this paper.

Only one out of every four or five sets of twins is monozygotic. The fertilized egg divides early in its existence; the cells resulting from this division are equivalent and totipotent and "each is capable of producing an entire creature exactly like that into which the entire egg should have developed." It is obvious that the innate constitutional endowments of monozygotic twins should be identical; their similarity should be manifest in their structural equipment and in their physiologic, emotional, and mental reactions. If one of the twins presents manifestations of a disease or an anomaly due to intrinsic factors, the other twin is expected to become a victim of the same process.

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The similarity of monozygotie twins is striking but only recently has it been brought out that a careful study of twins is as accurate as a study of the placenta in determining whether twins are monozygotie or dizygotie.<sup>8</sup> It is said that monozygotie twins have almost exactly the same number of finger ridges and the finger and sole prints are nearly identical. In this respect the hand of one monozygotie twin is as much like the hand of the other as are the two hands of the same person. Both Abt and Newman stated, however, that frequently one twin may be weak and defective, while the other is strong and vigorous. Dentition may occur at different times in the two babies; the handwriting of the two may be different.

Years ago, in speaking of twins, Galton said: "If anything ails one of them, identical symptoms nearly always appear in the other." Von Verschuer has found close correlation for the incidence and pathologic character of tuberculosis in monozygotie twins. Similar mental diseases have been reported in many pairs of twins, as have similar neurologic diseases, and Merriman has concluded that dementia praecox rarely occurs in only one of a pair of monozygotie twins. Wilson and Wolfsohn stated that identical twins show a striking similarity of structural, functional, and mental equipment and that organic nervous disease is probably the result of inherent defects which are present in both twins.

Similar anomalies and deformities also occasionally occur in each of monozygotie twins. Spina bifida, six fingers, cleft palate, and many other malformations have been described. Riba has reported the finding of a ureterocele in a symptom-free woman of 29 years of age who was examined because her twin sister was being treated for ureterocele and the concurrence of congenital anomalies in homologous twins was known by him.

In 1927 Twinem said that in every reported case in which a malignant tumor had occurred in one identical twin, it had occurred in the other as well, and the tumor had been of the same type and had involved the same organs. Warthin had said, according to Twinem, that up to that time only three cases of malignant tumor in identical twins had been reported. McFarland and Meade also said that there seemed to be no reported case in which a tumor was found in only one of homologous twins. They collected from the literature a series of forty tumors which had occurred simultaneously and symmetrically in twenty pairs of monozygotie twins. This study led them to suggest that "the origin of most tumors is to be found in the constitution of the sufferers and traced to a genetic source." In 1935 Militzer published a complete and interesting report of the simultaneous occurrence in twin brothers, aged 70 years, of carcinoma of the gastric cardia extending nearly to the pylorus. In 1936 Mumford and Linder reported



the finding of carcinoma of the left breast in each of female twins, aged 91 years. Only recently Phillips and Broders described the occurrence of carcinoma of both breasts in monozygotic twins and of papillary adenocarcinoma of the ovaries in one of the same pair of twins. They discussed the possibility of the appearance of carcinoma of the ovaries in the other twin.

The statements of Twinem and of McFarland and Meade to the effect that tumors and malformations never occur in only one of homologous twins have apparently stimulated interest in this subject. Wright reported cleft palate in one of identical twins. A case of schizophrenia in one of identical twins was described by Kasanin, but the environments of the twins were different. Dorff stated that Herrman had described a case of sporadic cretinism in one of male twins.

The only instance of acromegaly in twins was reported by Lewis in 1934. One of identical twin boys, aged 12 years, fell and struck his head. When he was 14 years of age he began to grow rapidly and soon exceeded his brother in height and strength. Since the cause of acromegaloid disease is not known and since this twin boy suffered an injury to his head, it is possible that this case should be placed in the same category as Love's case of subdural hematoma in a twin occurring shortly after birth.

To Kaplan belongs the distinction of reporting the only occurrence of carcinoma in one of homologous twins. In one of female twins, aged 51 years, who was similar in form and structure to her sister, he found carcinoma of the breast. Six years later no trace of malignant tumor could be found in the other twin. In this connection it is interesting to note that Champlin found sarcoma of the right testis in identical twins, the tumor occurring in one at the age of 24 years and in the other at 31 years of age. It is possible that a malignant tumor will yet develop in the unaffected twin who is being observed by Kaplan.

A case of acute myeloid leukemia in one of identical twin girls, aged 19 years, was described in 1937 by Kellett. Warren and Slipmer reported the finding of primary hyperplasia of the thyroid in one of stillborn twins whose mother had aborted after thyroidectomy. These few cases suffice to show that the appearance of anomalies and disease in only one of a pair of identical twins has been observed, although rarely.

A complete report of the occurrence of exophthalmic goiter in identical twin girls, aged 12 years, has been made by Neff. So far as I am able to learn, this is the only set of identical twins which has been afflicted with this disease. Wilson and Wolfsohn mentioned a set of twins who had "goitres." I can find no report of adenomatous or nodular goiters in monozygotic twins such as I wish to report.

## REPORT OF CASES

FIRST SET OF TWINS.—Twin girls, aged 12 years, presented themselves at the Mayo Clinic on April 15, 1919, because of enlargement of the thyroid glands. Their maternal grandmother and great-grandmother were said to have had goiters. The patients had always enjoyed good health and had had only measles and pertussis during childhood. The father thought that their necks had been full at birth and stated



Fig. 1.—Monozygotic twins, aged 15 years, whose goiters were first apparent at the age of 7 years.



Fig. 2.—The monozygotic twins shown in Fig. 1, at the age of 21 years. There has been a decrease in the size of the goiters, but the similarity is still striking.

that enlargement of the thyroids had been definite when the patients were 7 years old. The growth of the patients had been steady, with a marked increase in size during the six months preceding their admission to the clinic, and they were bright in school. The parents and the patients knew of no other case of thyroid dysfunction in the vicinity of their home.

On examination the first twin, Inez B., was found to be 5 feet, 3 inches (160 cm.) in height. She weighed 120 pounds (54 kg.). One tooth was carious and the tonsils and adenoids were slightly enlarged. Exophthalmos was questionable. The right lobe of the thyroid measured 2.5 by 4.3 inches (6 by 11 cm.); the left lobe measured 2.7

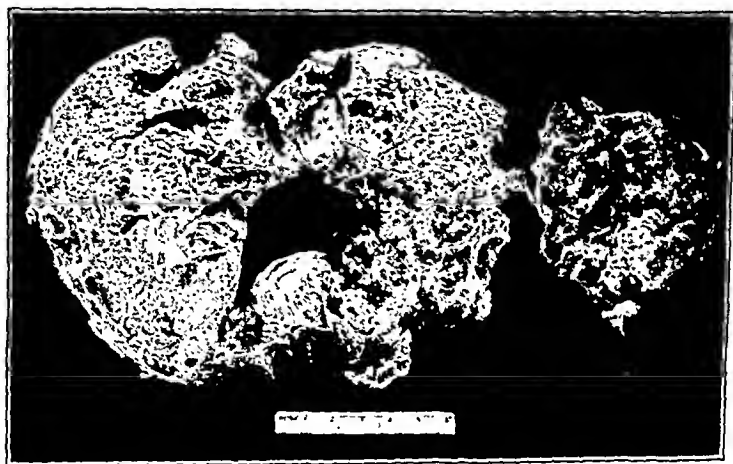


Fig. 3.—Specimen removed from the first patient shown in Fig. 1 (left). It measures 15 by 13 by 4 cm. and weighs 320 gm.



Fig. 4a and b.—Microscopic sections of specimens shown in Figs. 3 and 5. There is practically no difference in the microscopic pictures presented by the two specimens. Each shows colloid and fetal adenomas in a colloid thyroid.

by 4.5 inches (7 by 11 cm.). A thrill and bruit were heard at the right superior pole. The blood pressure was 112 mm. of mercury systolic and 71 diastolic. The concentration of hemoglobin (Dare) was 75 per cent and the leucocyte count 9,200 in each cubic millimeter of blood. Roentgenologic examination of the chest gave negative results. The basal metabolic rate was -9 per cent.

The second twin, Iva B., was 5 feet, 3 inches (160 cm.) in height and weighed 103 pounds (47 kg.). Her tonsils were also enlarged and her teeth also carious. The veins over the thyroid were dilated. The right lobe of the thyroid measured 2.7 by 4 inches (7 by 10 cm.); the left lobe measured 2.5 by 4 inches (6 by 10 cm.). The blood pressure was 120 mm. of mercury systolic and 80 diastolic. The concentration of hemoglobin (Dare) was 73 per cent and the leucocytes numbered 8,600 in each cubic millimeter of blood. Roentgenologic examination of the chest gave negative results, and the basal metabolic rate was -6 per cent.

Both patients were given thyroxine, 0.25 mg. daily, and were seen again in six weeks. The mother thought they had improved and that the glands were a little smaller, but the physical examinations were essentially the same as when first seen, and there had been no change in the basal metabolic rates.

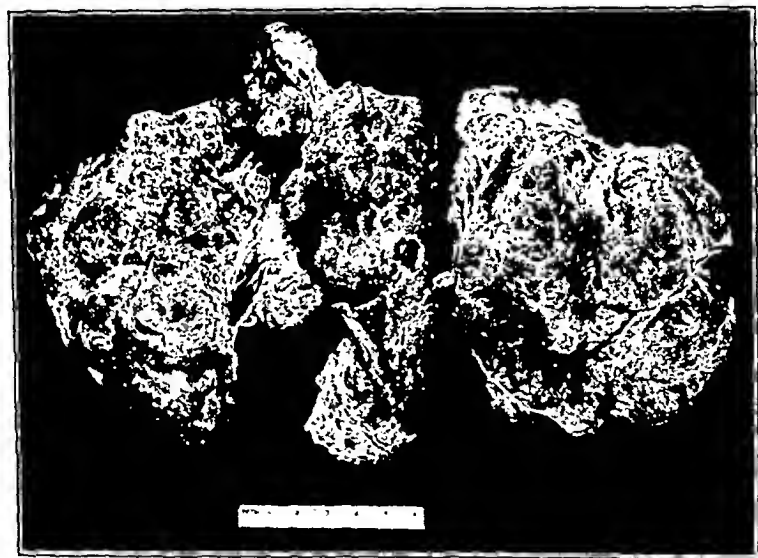


Fig. 5.—This specimen, removed from the second patient shown in Fig. 1 (right), measures 15 by 13 by 5 cm. and weighs 250 gm. In all details it is similar to the specimen shown in Fig. 3.

In June, 1922, the twins again came to the Mayo Clinic. Fig. 1 gives an idea of the similarity presented. They were 15 years of age at this time. Since their last visit they had suffered from influenza, and menstruation had been established. Inez B., the first twin, was found to be 5 feet, 5 inches (165 cm.) in height. She weighed 120.5 pounds (55 kg.). Two teeth were decayed. The superficial veins over the thyroid were dilated. A bruit and thrill were present on the right side of the gland, and a bruit was heard on the left side. The right lobe of the thyroid measured 4 by 5.5 inches (10 by 14 cm.); the left lobe measured 4.5 by 6 inches (11 by 15 cm.). The circumference of the neck was 21 inches (53 cm.). Roentgenologic examination of the chest gave negative results. On two occasions the basal metabolic rate was -2 per cent and -7 per cent.

The second twin, Iva B., was 5 feet, 5 inches (165 cm.) in height and weighed 112 pounds (51 kg.). The resemblance to her twin was striking (Fig. 1). The dil-

tation of the superficial veins over the thyroid made a pattern similar to that presented by her twin. The circumference of the neck was 20 inches (51 cm.). By measurement the right lobe of the thyroid was 4.5 by 4.5 inches (11 by 11 cm.) and the left 4 by 5.5 inches (10 by 14 cm.). A bruit was heard at the right superior pole. Basal metabolic rates were +5 per cent and -7 per cent.

Both patients were sent home with instructions to take desiccated thyroid gland. They were not seen at the Mayo Clinic again until January, 1928 (Fig. 2). The thyroid gland of Inez B., the first twin, measured 3 by 3.3 inches (8 by 8 cm.) on the right, and 3 by 3 inches (8 by 8 cm.) on the left. Roentgenologic examination of the chest gave negative results. The basal metabolic rate was -6 per cent. Dr. J. deJ.



Fig. 6.—Monozygotic twins, aged 38 years, who sought medical attention because of the enlargement of their necks.

Pemberton performed a subtotal thyroidectomy, with double resection and removal of the isthmus. The tissue removed (Fig. 3) measured 15 by 13 by 5 cm. and weighed 250 gm. The pathologist reported multiple hemorrhagic, fibrous, cystic, hyaline, granular, calcareous degenerating colloid and fetal adenomas in a colloid thyroid. A photomicrograph of the specimen is shown in Fig. 4a. Convalescence was uneventful and the patient was well when last heard from.

Iva B., the second twin, is shown with her sister in Fig. 2. A bruit was heard at the right lower pole of the thyroid. The enlarged gland measured 1.5 by 3 inches



Fig. 7.—Specimen removed from the first twin shown in Fig. 6 (left). It measures 6 by 6 by 4 cm. and weighs 55 gm.

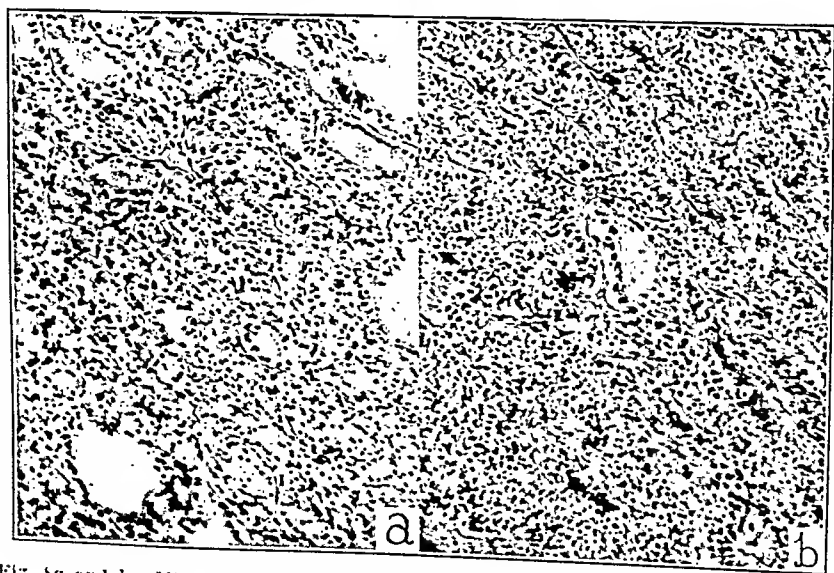


Fig. 8a and b.—Microscopic sections of the specimens shown in Figs. 7 and 9. Fetal adenomatous tissue predominates.

(4 by 8 cm.) on the right, 3 by 3 inches (8 by 8 cm.) on the left, and 3 by 3.5 inches (8 by 9 cm.) in the center. The basal metabolic rate was -3 per cent. This patient was operated upon on the same day as her twin sister. A subtotal thyroidectomy with double resection and removal of the isthmus was performed by Dr. J. deJ. Pemberton. The tissue removed was almost indistinguishable from that removed from the twin sister. Its size was 15 by 13 by 4 cm. and its weight was 320 gm. Fig. 4b is a photomicrograph and Fig. 5 a photograph of the specimen. The pathologist's report was multiple hemorrhagic, fibrous, cystic, hyaline, granular, calcareous, degenerating colloid and fetal adenomas in a colloid thyroid. Convalescence was smooth and the patient was dismissed with her sister.

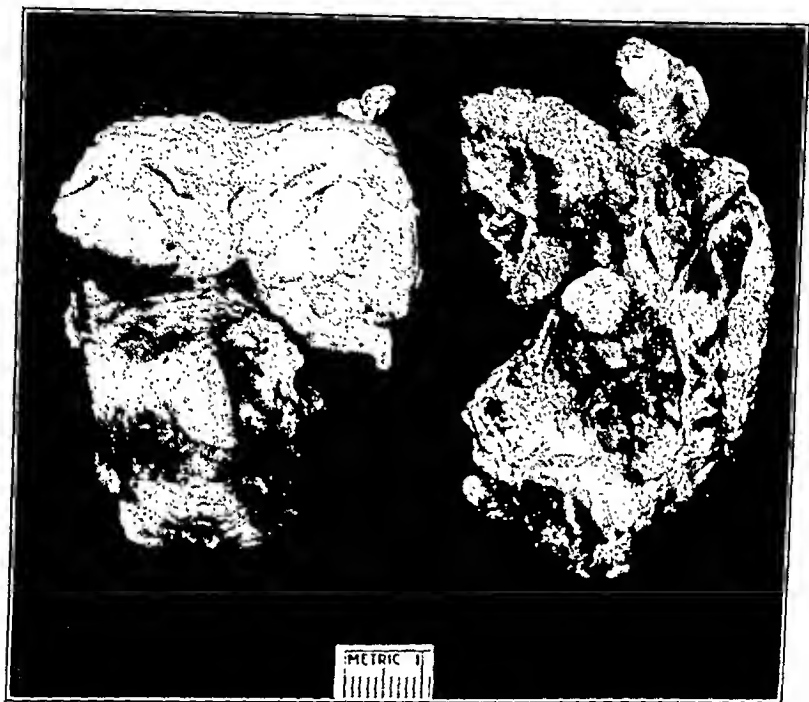


Fig. 9.—This specimen, removed from the second twin shown in Fig. 6 (right), measures 7 by 4 by 3 cm. and weighs 40 gm. It is grossly and microscopically indistinguishable from the specimen removed from the other twin.

**SECOND SET OF TWINS.**—The second set of twins was observed first in December, 1936. They were single women, aged 38 years, who said that they had always looked very much alike, but the similarity was greater when they were children. Each complained of a swelling in her neck. Fig. 6 is a photograph of the twins as they appeared when first seen.

The first twin, K. W., had noticed the increase in the size of her neck five years before coming to the Mayo Clinic. Since that time the enlargement had been gradual and there had been a "heavy feeling" in her neck. For two weeks she had taken iodine. Her height was 5 feet, 5 inches (165 cm.). She weighed 150 pounds (68 kg.). The thyroid gland was enlarged and nodular. The blood pressure was 144 mm. of mercury systolic and 90 diastolic. Blood studies were normal and the flocculation reaction for syphilis was negative. The basal metabolic rate was +15 per cent.

On Dec. 15, 1936, Dr. C. F. Dixon did a subtotal thyroidectomy. It was noted that the right lobe of the thyroid was enlarged to about three times normal size and

the left lobe to five times normal size. The tissue removed measured 6 by 6 by 4 cm. and weighed 55 gm. A photograph of the specimen is reproduced in Fig. 7. The pathologist reported multiple hemorrhagic, degenerating, fibrous, hyaline, calcareous, cystic fetal and colloid adenomas in a colloid thyroid. A photomicrograph of the tissue is shown in Fig. 8a.

The second twin in this set, Z. W., had become aware of the swelling in her neck about a year before examination at the Mayo Clinic. She complained of a tight sensation in her neck and of occasional palpitation of the heart. Her height was also 5 feet, 5 inches (165 cm.) and her weight was 136 pounds (62 kg.). The thyroid gland was enlarged and nodular, with the greatest enlargement on the left side. The blood pressure was 124 mm. of mercury systolic and 78 diastolic. Blood examinations gave normal results. The flocculation reaction for syphilis was negative and the basal metabolic rate was +17 per cent.

Dr. C. F. Dixon performed subtotal thyroidectomy on Dec. 15, 1936, soon after completion of thyroidectomy on the twin sister. It was observed that the anterior jugular veins of the two patients were mirror images of one another. In the first patient the left anterior jugular vein was 1 to 2 mm. in diameter and the right was about 6 mm. in diameter, while the proportions were reversed in the patient's twin. The right lobe of the thyroid was enlarged to three times normal size and the left lobe to five times normal size. The surgical specimen was 7 by 4 by 3 cm. in size and weighed 40 gm. Examination of the tissue, a photograph of which is reproduced in Fig. 9, revealed multiple hemorrhagic, fibrous, degenerating fetal and colloid adenomas in a colloid thyroid. A photomicrograph of the tissue is shown in Fig. 8b. Both patients made a satisfactory convalescence and were enjoying good health when last heard from.

#### COMMENT

Heredity, age, sex, social status, economic conditions, hygiene and dietary insufficiencies, and inability to utilize iodine have been mentioned as having a causal relationship to nodular goiter. There are some who maintain, as did Wolfer, that adenomas of the thyroid develop from embryonal rests, while others consider nodules in the thyroid gland the result of a process of irregular hyperplasia and involution. At the present time it is not possible to select the cause of nodular goiter, but one can state with certainty that the causative forces were operating simultaneously and with approximately equal intensity in each of the two sets of twins reported. The gross specimens and the microscopic sections present nearly identical pictures.

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## THE SURGICAL TREATMENT OF BILATERAL BRONCHIECTASIS. WITH REPORT OF A CASE OF BILATERAL LOBECTOMY

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**S**URGICAL extirpation of the affected lobes is the only procedure that offers hope of a permanent effective cure in the treatment of bilateral bronchiectasis. We realize that this is radical treatment, but we believe that the results obtained so far indicate that this procedure may be carried out with a mortality not much higher than that obtained in unilateral disease. Before advocating a procedure as formidable as bilateral lobectomy, we have fully satisfied ourselves that no other proposed method of treatment can permanently relieve these patients. This disease is chronic and debilitating and is one whose features are such that those afflicted are not only physically but also mentally ill. The putrid expectoration and fetid breath which are so often present in the septic phase of bronchiectasis make the unfortunate victim a true social outcast, barred from all normal intercourse with his fellow creatures. Many have expressed a preference for death rather than life under these conditions. Added to the mental and psychic disabilities incurred are physical risks of the gravest sort. Hemoptysis, empyema, fatal metastatic cerebral abscess, acute pneumonia, and amyloidosis are the more severe complications. Severe and recurrent acute respiratory infections, especially in the winter months, serve to keep most of these patients from steady employment. A fact not generally appreciated is that untreated and even medically treated bronchiectasis progresses to a fatal termination in a large percentage of cases. Warner<sup>1</sup> found that 23 per cent of his cases were dead after an average duration of the disease of 9 years. Findlay and Graham<sup>2</sup> state that the disease shows no tendency to heal and that cases with a long history tend to get worse. They believe that the preponderance of bronchiectasis in children and young adults possibly may be explained on the assumption that persons with bronchiectasis do not live to adult or middle life. Clark<sup>3</sup> estimated the duration of life after development of the disease at 11.8 years. Of 23 cases studied by Findlay and Graham, 4 died of complications of the disease, 2 of septic pneumonia, 1 of hemoptysis, and 1 of brain abscess. Rist<sup>4</sup> emphasizes that bronchiectasis is an incurable and deadly disease, which after a longer or shorter period eventually kills and which, therefore, should be treated as early and as effectively as possible.

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The place of lobectomy in the treatment of bronchiectasis is established and accepted. The mortality of the operation has dropped from 55 per cent in 1929 to an average today of 10 to 15 per cent in good clinics. Selected series show an even lower death rate. We feel that while careful selection of cases is advisable during the developmental stage of an operation of the magnitude of lobectomy the time has come when the indications for operation should be broadened. The profession has been made fully aware of the fact that unilateral cases of



Fig. 1.—Iodized oil x-ray taken on March 17, 1937, showing bilateral lower lobe bronchiectasis.

bronchiectasis can be cured of their disease by surgical extirpation of the affected lobe, with a high margin of safety. However, the feeling still persists that the bilateral case is beyond the scope of surgical treatment. As a consequence many sufferers from this dangerous, debilitating disease are denied the opportunity of being cured by operation. There are few published reports of lobectomy in the treatment of bilateral bronchiectasis, although we are sure that they are being accepted for operation in most clinics today. Churehill in 1937 reported 5 lobectomies in bilateral cases with 1 death and with marked improvement in

the surviving 4. Whether subsequent operations have been done to remove the contralateral affected lobes in these cases we do not know. This author states that there should be no hesitancy in advising bilateral operations if necessary. During the past two years we have performed 12 lobectomies in cases with bilateral disease with 2 deaths, a case mortality of 16.6 per cent. Death in one of these patients we feel was directly attributable to a transfusion reaction which took place on the operating table. Acute pulmonary edema was the immediate cause of death. Eliminating this one case, we arrive at a mortality of 9 per cent. It should be emphasized that these cases were entirely unselected and most of them had extensive disease.



Fig. 2.—X-ray taken seven weeks after second lobectomy. A slight amount of fluid and a small encapsulated pneumothorax are present at the right base. The left upper lobe and the right middle and upper lobes are well expanded.

Having demonstrated the practicability and comparative safety of operation in bilateral bronchiectasis, we are faced with the problem of handling these patients after one lobe has been removed. It has been our experience that those patients with minimal changes in the remaining affected lobe may be entirely symptom free after removal of the

more severely infected lobe. Three of our cases in this category have been entirely symptom free since lobectomy. The follow-up in these three cases has been respectively ten, eleven, and seventeen months. Five cases have shown marked improvement and are waiting to have the other infected lobe removed. One patient who had the left lower lobe and lingula of the upper lobe removed is still in the hospital with a residual empyema and has shown progression of the disease in her right middle lobe. Two patients have died. One young man with disease of both lower lobes has undergone bilateral lower lobe lobectomy and is symptom free ten months after removal of the second lobe.



FIG. 3.—Left lower lobe, removed on March 25, 1937.

A rather cursory review of the literature has revealed only three other cases on record in which bilateral lobectomy has been successfully accomplished, those of Eloesser,<sup>6</sup> Lewis,<sup>7</sup> and Overholt.<sup>8</sup> We believe it important that these cases be placed in the literature to bring to the attention of the medical profession the fact that bilateral bronchiectasis can be treated surgically and that the prognosis of operation is far from hopeless. It is interesting to note in Overholt's case that the vital en-

capacity and lung volume were greater after both operations. In our own case the course after the second lobectomy was much smoother than after the first operation. This is to be expected since there is usually great improvement in the general health after removal of the more severely affected lobe and also the risk of aspirating pus from an infected lobe into normal lung tissue is not present at the second operation.

Certain features in the management of these patients should be stressed. Careful preoperative lung mapping with iodized oil is imperative. Each lobe should be injected and x-rayed separately with special attention being paid to proper bronchographic technique. These points have been brought out in articles by Goldman and Adams<sup>9</sup> and Hasley and Hudson.<sup>10</sup> Adequate bronchoscopic and postural drainage preoperatively lessens the risk of aspiration of pus during operation.



Fig. 4.—Right lower lobe, removed on Dec. 6, 1937.

We have used endotracheal anesthesia in all our cases since we feel that the advantages of endotracheal suction in bilateral cases far outweigh its disadvantages. We endeavor to have all our cases in the best possible general health and gaining weight at the time of operation. Fever or recent attacks of bronchitis or pneumonitis are considered contraindications to operation.

A brief case report of the patient who has successfully survived removal of both lower lobes is appended.

## CASE REPORT

J. V., male, aged 23 years, was admitted to Jefferson Hospital on March 13, 1937, complaining of cough and the expectoration of about 3 ounces of pus daily. His symptoms dated back six years and began after a series of acute upper respiratory infections. Bronchoscopic examination by Dr. Louis H. Clerf showed purulent secretion coming from both lower lobe bronchi. Repeated bronchograms over a period of one year demonstrated progressive cylindrical bronchiectasis in both lower lobes, more advanced on the left. On March 25, 1937, a one-stage resection of the left lower lobe was done under nvertin-endotracheal cyclopropane anesthesia. A moderate number of pleural adhesions were present. Drainage was established by means of an intercostal tube which was immediately connected to a suction pump, keeping a constant negative pressure in the pleural cavity. His convalescence proceeded uneventfully except for an acute type IV pneumococcus pneumonia which developed in the right middle lobe on May 2, 1937. He made a satisfactory recovery from this and was discharged on May 21, 1937, with all symptoms improved.

On Nov. 29, 1937, he was readmitted for the second operation. His general condition was greatly improved; he had gained weight and had much less cough and expectoration. X-ray of the left chest showed good expansion and aeration of the left upper lobe and elevation of the left diaphragm. A bronchogram of the right lung showed a slight progression of the lower lobe bronchiectasis.

On Dec. 6, 1937, under endotracheal cyclopropane-ether anesthesia, a one-stage right lower lobectomy was performed. The lobe was moderately adherent. Intercostal drainage was used and negative pressure applied. The patient developed a postoperative empyema which was effectively drained through the intercostal tube. He was discharged fully healed on Feb. 10, 1938. At the present time he is gaining weight, is cough and sputum free, and is back at his previous occupation.

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## SCALENUS ANTICUS SYNDROME

### A DIAGNOSTIC AND CONFIRMATORY TEST

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**S**CALENUS anticus syndrome is a definite clinical entity, characterized by the clinical manifestations of neurocirculatory disturbances, resulting from compression of both the brachial plexus and the subclavian artery by the scalenus anticus muscle.

In 1934, in conjunction with Ochsner and DeBakey,<sup>1</sup> I described the clinical manifestations and treatment of scalenus anticus syndrome and reviewed the theories explaining the etiology. It was demonstrated in that communication that spasm of the scalenus anticus muscle was present in all cases presenting the syndrome, and it was suggested that the spasm was a major factor in producing the symptoms.

That only a small percentage (9 per cent) of patients with cervical ribs manifest clinical symptoms has been demonstrated conclusively by Torelli.<sup>2</sup> Only 9 of 100 cases of cervical ribs which he reported produced symptoms. Therefore the symptoms are not due primarily to the cervical rib but are dependent upon some other factor, which we believe is spasm of the scalenus anticus muscle.

Those cases that have the clinical manifestations of cervical rib without a cervical rib being present have been designated by Naffziger<sup>3</sup> and by myself<sup>1</sup> as scalenus anticus syndromes, and by Spurling and Bradford<sup>4</sup> as scalenus neurocirculatory compressions. The same etiologic factor responsible for the symptoms of cervical rib is also present in the cases without cervical rib. This factor we believe is a definite spasm of the scalenus anticus muscle. As previously stated, it is our opinion that there is a definite vicious circle that is responsible for the production of symptoms in this interesting clinical entity.<sup>1</sup> This consists of spasm of the scalenus anticus muscle (probably from trauma), which in turn elevates the first rib and compresses the brachial plexus, which increases the spasm of the scalenus anticus muscle by reflex irritation of the nerve supply to the muscle. If the patient elevates the arm above the head, the symptoms are relieved; i.e., relaxation of the scalenus anticus muscle occurs.

If one can completely eliminate the muscle spasm, the vicious circle is broken and the symptoms are permanently relieved. It is upon this premise that section of the scalenus anticus muscle for the cure of the disease is based. The severance of the muscle breaks the vicious circle and permanently destroys the compressive effect on the brachial plexus



## CASE REPORT

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border of the scalenus anticus muscle, a needle is inserted into its lateral edge (Fig. 1). The muscle is then infiltrated with 1 per cent novocain through its lower half, care being taken not to infiltrate the phrenic nerve or brachial plexus. Within five to ten minutes the scalenus anticus muscle is completely relaxed and the patient is temporarily relieved of the symptoms.\*

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\*On Jan. 19, 1939, I performed the diagnostic test on a patient who was suffering with pain in neck and arm secondary to a cervical rib on the right side. The patient was completely relieved temporarily following injection of the scalenus anticus with 1 per cent novocain.

and the subclavian artery by the scalenus anticus muscle. Therefore, it is believed that both of these interesting clinical entities are produced by spasm of the scalenus anticus muscle.

If this premise is correct, then the relief of the spasm of the scalenus anticus muscle by novocain injection not only would give temporary relief of the symptoms but would be of diagnostic importance in confirming the diagnosis of scalenus anticus syndrome with and without the presence of a cervical rib.



Fig. 1.—Injecting scalenus muscle with novocain avoiding phrenic nerve and brachial plexus.

I had the privilege recently of demonstrating the presence of spasm of the scalenus anticus muscle in two patients who presented definite clinical manifestations of scalenus anticus syndrome. The scalenus anticus muscle was injected with 1 per cent novocain which completely relieved the symptoms for a period of eight hours in one case and four hours in the other. One case was operated upon and the scalenus anticus muscle was found to be hypertrophied and rather firm in texture and was tightly compressing the brachial plexus. Section of the muscle completely relieved the patient of her symptoms.

I offer this test (blocking the scalenus anticus muscle with novocain) as a diagnostic aid in confirming the diagnosis of scalenus anticus syndrome with and without the presence of a cervical rib. The diagnostic test is performed as follows: With the patient in the recumbent position, the head is turned toward the unaffected side. The scalenus anticus muscle is palpated behind and lateral to the sternomastoid muscle. With the index finger of the left hand palpating the lateral

lesion has been seen in patients as young as 14 years of age<sup>23</sup> and several cases are reported in patients below 30 years. In their studies on aneurysms of the hepatic artery Friedenwald and Tannenbaum<sup>6</sup> conclude that infectious processes in the body were far more important than syphilis as etiologic factors. If this is true of the hepatic artery, it is probably also true of the splenic. Septic emboli probably account for a certain percentage of splenic aneurysms, although these are rare according to Eppinger.<sup>23</sup> Trauma appears to have been a factor in several cases, as in that of Marshall,<sup>19</sup> who reported a splenic aneurysm following a bullet wound near the artery. Periarteritis nodosa as a cause of aneurysms is commented on by Harris and Friedrichs<sup>10</sup> and Singer.<sup>27</sup> Congenital aneurysms are rare<sup>14</sup> and I found no convincing report of one of the splenic artery.

The association of ruptured splenic aneurysms with pregnancy is worthy of comment. My Case 1 was that of a woman 25 years of age who was in her fifth month of pregnancy. Sered and Steiner<sup>26</sup> reported a case of a woman 30 years of age at full term who was delivered by cesarean section of a live child shortly before death from hemorrhage from a ruptured 15 mm. aneurysm in the midportion of the splenic artery. They believed this to be of a congenital origin. Von Rooy,<sup>30</sup> Landwall and Gödl,<sup>17</sup> Mayer,<sup>26</sup> Remmelts,<sup>23</sup> Wesenberg,<sup>31</sup> and Saenger<sup>24</sup> all reported somewhat similar cases, with deaths of the mothers. These 8 cases constitute about 12 per cent of all reported cases, a significant proportion.

The symptoms of splenic aneurysm, as judged by case reports, are variable and none are pathognomonic. Pain in the epigastrium or left upper quadrant, frequently sudden and severe but often chronic and colicky, is most common. Attacks of vomiting with hematemesis and melena are frequent. A tumor mass is occasionally present. Many of the patients have an unheralded, sudden, severe intra-abdominal hemorrhage as the first symptom and are in a moribund condition when first examined by a physician.

The diagnosis was made correctly before operation in only 2 cases. Höglér<sup>12</sup> made it on the basis of left upper quadrant pain, a lesser curvature pulsating filling defect of the stomach, and a systolic bruit over a palpable tumor mass. Lindboe<sup>15</sup> also made a correct preoperative diagnosis by means of the x-ray. Ahrens<sup>1</sup> and Heppner<sup>11</sup> reported a pulsating mass in each of their cases. Brockman<sup>4</sup> heard a bruit in the left upper quadrant in his patient. Later the bruit disappeared. He concluded that there occurs first a primary rupture of the aneurysm into the lesser peritoneal cavity or splenic pedicle, which destroys the bruit. At a later date a secondary and fatal hemorrhage occurs into the abdominal cavity. Bertrand and Clavel<sup>3</sup> also believed the rupture usually occurred in two or more stages. Brockman emphasized the value of auscultation in the diagnosis of the acute abdomen. Cabot<sup>5</sup>

## ANEURYSM OF THE SPLENIC ARTERY

### REVIEW OF THE LITERATURE AND REPORT OF TWO CASES

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**A**LTHOUGH intra-abdominal aneurysms are unusual, especially those of the branches of the aorta, they occur with sufficient frequency to merit consideration in the diagnosis of certain obscure abdominal disorders. In the interest of more accurate diagnosis, especially in view of our increasing knowledge of vascular phenomena, it seems worth while to review the literature on splenic artery aneurysms and to report two additional cases.

An aneurysm of the splenic artery is found in about every 1,500 autopsies. Schraeder<sup>22</sup> collected records of 20 cases in 32,768 autopsies (1 in 1,600) in Europe; and Garland<sup>7</sup> records 3 found in over 4,100 autopsies (1 in 1,400) in Boston. Muller<sup>21</sup> found 9 in 10,360 autopsies (1 in 1,150), and the 2 herewith reported were the only ones seen by myself in a series of over 5,000 autopsies (1 in 2,500). In 1929 Anderson and Gray<sup>2</sup> collected 58 cases and wrote an excellent summary of existent knowledge of the lesion. At about the same time, Friedenwald and Tannenbaum<sup>6</sup> collected from the literature 65 cases of aneurysm of the hepatic artery and Singer<sup>23</sup> 40 cases of aneurysm of the renal artery. McNealy<sup>18</sup> recognized their significance when he stated that "aneurysms of the splenic and renal arteries are the most common visceral aneurysms which come to surgical attention."

The etiologic factors in aneurysms of the splenic artery are worthy of note. Its anatomic position in loose areolar retroperitoneal tissue along the upper border of the pancreas allows for a certain freedom of motion of this vessel which probably helps explain its frequent tortuosity. This may be extreme and it is of interest that anatomists<sup>9</sup> have regarded this tortuosity as a normal condition of the vessel. Springorum<sup>25</sup> concluded that the degree of tortuosity bore no relation to the age of the patient but was due to an increase in length of the vessel resulting from toxic factors on the walls or from enlargement of the spleen. He found that nodose arteriosclerosis occurred on the convex side of the bends in the vessel and was a result of the tortuosity. This is of significance as some degree of atherosclerosis is described in the splenic artery in the majority of the reported cases and suggests that degenerative changes are the most important factor in the development of splenic aneurysms. My Case 2 is of this type.

The importance of syphilis in the etiology of splenic aneurysms is difficult to evaluate. Certainly in the majority of the reported cases no mention is made of any other evidences of syphilis in the body. The

lesion has been seen in patients as young as 14 years of age<sup>29</sup> and several cases are reported in patients below 30 years. In their studies on aneurysms of the hepatic artery Friedenwald and Tannenbaum<sup>6</sup> conclude that infectious processes in the body were far more important than syphilis as etiologic factors. If this is true of the hepatic artery, it is probably also true of the splenic. Septic emboli probably account for a certain percentage of splenic aneurysms, although these are rare according to Eppinger.<sup>13</sup> Trauma appears to have been a factor in several cases, as in that of Marshall,<sup>19</sup> who reported a splenic aneurysm following a bullet wound near the artery. Periarteritis nodosa as a cause of aneurysms is commented on by Harris and Friedrichs<sup>10</sup> and Singer.<sup>27</sup> Congenital aneurysms are rare<sup>14</sup> and I found no convincing report of one of the splenic artery.

The association of ruptured splenic aneurysms with pregnancy is worthy of comment. My Case 1 was that of a woman 25 years of age who was in her fifth month of pregnancy. Sered and Steiner<sup>26</sup> reported a case of a woman 30 years of age at full term who was delivered by cesarean section of a live child shortly before death from hemorrhage from a ruptured 15 mm. aneurysm in the midportion of the splenic artery. They believed this to be of a congenital origin. Von Rooy,<sup>30</sup> Lundwall and Gödl,<sup>17</sup> Mayer,<sup>20</sup> Remmelts,<sup>23</sup> Wesenberg,<sup>31</sup> and Saenger<sup>24</sup> all reported somewhat similar cases, with deaths of the mothers. These 8 cases constitute about 12 per cent of all reported cases, a significant proportion.

The symptoms of splenic aneurysm, as judged by case reports, are variable and none are pathognomonic. Pain in the epigastrium or left upper quadrant, frequently sudden and severe but often chronic and colicky, is most common. Attacks of vomiting with hematemesis and melena are frequent. A tumor mass is occasionally present. Many of the patients have an unheralded, sudden, severe intra-abdominal hemorrhage as the first symptom and are in a moribund condition when first examined by a physician.

The diagnosis was made correctly before operation in only 2 cases. Höglér<sup>12</sup> made it on the basis of left upper quadrant pain, a lesser curvature pulsating filling defect of the stomach, and a systolic bruit over a palpable tumor mass. Lindboe<sup>15</sup> also made a correct preoperative diagnosis by means of the x-ray. Ahrens<sup>1</sup> and Heppner<sup>11</sup> reported a pulsating mass in each of their cases. Brockman<sup>4</sup> heard a bruit in the left upper quadrant in his patient. Later the bruit disappeared. He concluded that there occurs first a primary rupture of the aneurysm into the lesser peritoneal cavity or splenic pedicle, which destroys the bruit. At a later date a secondary and fatal hemorrhage occurs into the abdominal cavity. Bertrand and Clavel<sup>7</sup> also believed the rupture usually occurred in two or more stages. Brockman emphasized the value of auscultation in the diagnosis of the acute abdomen. Cabot<sup>5</sup>

described the case of a 74-year-old woman who had a sudden rupture of a splenic aneurysm as determined at autopsy. Operation revealed about 1,000 c.c. of blood in the abdomen, yet the preoperative examination had revealed audible peristaltic sounds. He records the opinion of Reginald Fitz, Sr., that some cases thought to be acute hemorrhagic pancreatitis may be examples of pancreatic apoplexy due to the rupture of a sclerotic vessel. Goodheart<sup>1</sup> heard a murmur in his patient. Lower and Farrell<sup>16</sup> call attention to the fact that auscultation is usually omitted in the abdominal examination. They reported the case of a 16-year-old boy who had had recurring attacks of severe abdominal pain following whooping cough eight years previously. At operation an aneurysm was found adherent to the tail of the pancreas which was resected with the aneurysm. The patient recovered. They add one more diagnostic sign which was present in their case, a pancreatic deficiency as evidenced by undigested fat in the stool. Osborne's<sup>22</sup> patient, a woman 43 years of age, gave a history of attacks of colicky pain aggravated by stooping, and he believes that an alteration of the intensity of the pain with postural changes suggests a vascular lesion.

The treatment of splenic aneurysms was summarized by Lower and Farrell<sup>16</sup> who stated that ligation of the vessels or splenectomy is of major importance. Ligation of the artery is followed by aseptic atrophy of the spleen which is without serious ill effects. Tamponage is ineffectual and all patients died when this method alone was used to control the hemorrhage. They reviewed 7 cases which recovered following operation and added 1 of their own. Lindboe's patient<sup>13</sup> also lived, making a total of 9 recoveries reported to date in patients who have been operated upon for the condition.

The following 2 cases of splenic aneurysm illustrate well the extremes in age and etiology under which the lesion may be found.

#### CASE REPORTS

CASE 1.—This 25-year-old Irish housewife was five months pregnant and had been receiving prenatal care from a physician who reported her heart, blood pressure, and urine as normal two weeks before her final day of illness. On that day she did the family washing and went for an evening walk. On her return home she suddenly complained of pain across the upper abdomen. She retired and the pain steadily increased, with vomiting, but no hematemesis or melena. She was dead at the time of the arrival of her physician, about two and one-half hours after the onset of her illness. His diagnosis was ruptured tubal pregnancy.

Post-mortem examination revealed a well-developed and nourished female with no marks of external violence. The abdominal cavity contained over 5,000 c.c. of clotted and fluid blood. The uterus was pregnant with a normally developed placenta and 25 cm. (five months') female fetus. In the left upper abdominal quadrant was a huge mass of soft clotted blood 12 to 14 cm. in diameter. The blood clot infiltrated the omentum, the wall of the left half of the transverse colon, the pedicle of the spleen, surrounded the tail of the pancreas, extended to the hilum of the left kidney, and filled the lesser peritoneal cavity. The retroperitoneal tissues were free of blood.

The spleen weighed 189 gm. and measured 14 by 8 by 2 cm. The splenic artery averaged 9 mm. in circumference and was slightly tortuous throughout but free from atheromatous changes or other abnormalities until it reached the hilum of the spleen. Here it was narrowed to a circumference of 7 mm. by a constricting ring 2 mm. wide. Immediately distal to this constriction the vessel opened into an aneurysmal sac 2 cm. long by 1 cm. in diameter in the wall of which was a round, yellow, flat, firm, atheromatous plaque 7 mm. in diameter. The plaque and the sac elsewhere were lined by smooth endothelium. Immediately distal to the constricting



Fig. 1.—Case 1. The splenic artery (A) is shown with the constricting ring at the opening into the aneurysmal sac (B). The perforation of the aneurysm is shown at C.

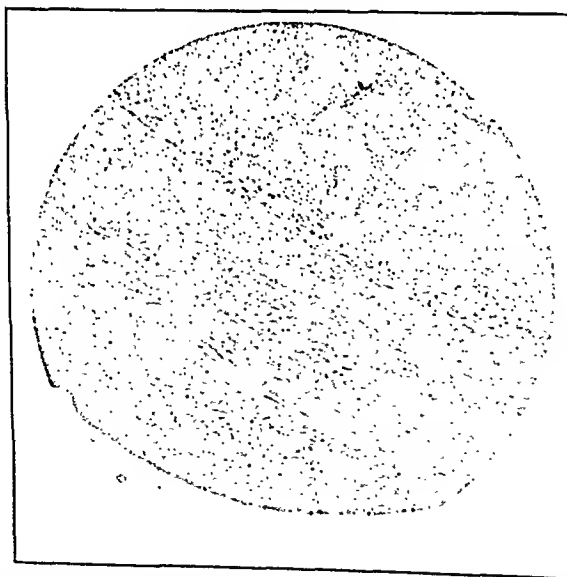


Fig. 2.—Case 1. Photomicrograph of the atherosclerotic plaque in the wall of the aneurysmal sac. Evidences of inflammatory changes are absent.



ring a small artery 6 mm. in circumference arose from the sac and extended to the spleen. This small artery was tortuous and the lining of its proximal 7 mm. was dotted with tiny yellow atheromatous patches up to 1 mm. in size. Adjacent to this vessel on the lateral wall of the aneurysmal sac was an irregularly round perforation 9 mm. in diameter. Adherent to its edges was a fringe of soft friable yellow brown tissue 2 mm. thick. The cavity of the aneurysmal sac communicated through this opening with an irregular space 3 cm. long and 1 to 1.5 cm. in diameter which extended to the capsule of the spleen and merged into the surrounding blood clot. This space was lined by a thin, delicate, and readily torn fibrinous membrane. The sac and this space were surrounded by a firm, red-brown, friable mass of clotted blood which infiltrated the gastrosplenic omentum and was loosely adherent to the splenic capsule. The capsule was smooth and glistening except for adherent recent blood clots and a 6 by 1 cm. fibrous diaphragmatic adhesion on the superior aspect. The splenic pulp was soft, gray-red, with indistinct corpuscles. There were no infarctions of the pulp. The splenic vein was buried in blood clots but its lining was normal.

The heart was normal in size and the endocardial and pericardial surfaces were all smooth and glistening. The myocardium was soft, brown, unscarred, and of normal thickness. The valves were all normal except the posterior leaflet of the mitral. Here on the line of closure was a row of five tiny 1 mm. granular deposits. There were a few small scattered yellow patches in the descending aorta but no ulceration or calcification of this vessel. The other organs showed anemia but no other essential abnormalities.

The opened aneurysmal sac and spleen are shown in Fig. 1. The microscopic appearance of the atherosclerotic patch in the wall of the aneurysm is seen in Fig. 2. Microscopic study of the vessel at the point of rupture showed no definite evidences of inflammation, but the hemorrhagic infiltration was sufficient to obscure any which may have been present. Smears of the mitral and aneurysmal vegetations showed no bacteria. Cultures could not be made.

CASE 2.—This 65-year-old white male died in St. Bernard's Hospital on the service of Dr. J. T. Meyer. He entered with a urethral stricture, suppurative prostatitis, and ascending urinary infection and died suddenly of pulmonary embolism ten days following suprapubic cystotomy. He admitted having had gonorrhea eighteen years previously but denied syphilis. The blood Wassermann was negative.

Post-mortem examination revealed the pulmonary embolism, a thrombosed right femoral vein, and severe urinary tract infection. There was a marked atherosclerosis of the aorta, coronary arteries, and ulceration of the descending aorta. No aneurysmal dilatations and no gross evidences of syphilis were found in any of these vessels. The aneurysm of the splenic artery was an incidental finding in this body.

The splenic artery arose normally from the celiac. It lay in a loose areolar and fatty tissue and was markedly tortuous. The walls averaged about 1 mm. in thickness, but the internal lining was almost completely altered by gray to yellow scars and patches up to 6 mm. in diameter. These patches were mainly of the atheromatous type, and a few were superficially ulcerated with a slight amount of calcification. There were many tiny pits in the intima and considerable longitudinal wrinkling but no areas clearly recognizable as altered by syphilitic infection. The circumference of the vessel varied from 1.5 to 2.5 cm.

Four centimeters from the hilus of the spleen there was a saecular out-pouching from the superior anterior surface of the splenic artery. This mass measured 2.3 by 2 by 1.6 cm. and had a tough fibrotic wall 1 to 2 mm. thick. The wall was a gray pink with a central thin pale yellow layer. The sac was lined by soft yellow atheromatous material and firmly adherent blood clots. It was filled completely by old brown to yellow, friable, clotted blood. Its cavity communicated with the lumen

of the splenic artery by a smooth edged constricted opening 1.3 by 1 cm. in size. About this opening the walls of the artery were particularly firm and scarred.

The aneurysm was surrounded by nonadherent loose fatty tissue and its anterior surface was adjacent to and somewhat compressed the pancreas in a 1.5 cm. area. There were no visible abnormalities of the pancreas at this point, however. The whole pancreas was of normal size, firm, and about one-third replaced by fat. The splenic artery distal to the aneurysm was essentially similar to the proximal portion. The spleen was about twice normal size, weighed 230 gm., was free of adhesions, had a smooth capsule and a dark purple, firm pulp with prominent Malpighian capsules. There were no scars or other evidences of old or recent infarction.



Fig. 3.—Case 2. On the left is seen an opened segment of the tortuous sclerosed splenic artery. The aneurysmal sac and pancreas have been bisected. The constriction of the artery where it enters the sac is apparent.

Fig. 3 shows a segment of the splenic artery and the bisected aneurysmal sac with adjoining pancreas. Microscopic examination of the walls of the sac revealed an absence of the intima with fibrinous blood clots adherent to a fibrotic and distorted media. In this layer there were a few scattered round cells but no perivascular collections. The adventitia was essentially normal. Sections of the main splenic artery and of the aorta revealed no evidences of syphilis.

#### CONCLUSION

Two cases of aneurysm of the splenic artery are reported.

One in a woman 25 years of age was probably of mycotic origin from an endocarditis. It ruptured spontaneously, causing death within three hours. The patient was five months pregnant. Records were found of 7 other similar cases of ruptured splenic aneurysms in pregnancy.

Another was due to arteriosclerosis and was an incidental finding at autopsy in a male 65 years of age who died of a urinary tract infection.

The subject is reviewed to emphasize the salient points in etiology, symptomatology, diagnosis, and treatment of the condition.

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# CHRONIC SCIATIC PAIN DUE TO ADHESIONS ABOUT THE NERVE TRUNK AND THE RESULTS OF THEIR REMOVAL BY OPERATION\*

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**A**MONG those who suffer from sciatica is a group whose pain can be relieved only by operation. Renton,<sup>1</sup> Pers,<sup>2</sup> and Taylor<sup>3</sup> have called attention to this procedure. This paper gives the results of 28 operations upon 24 patients, performed between 1925 and 1937. These patients constitute a selected group.

## ANATOMY

For practical purposes, the sciatic nerve must be considered as extending from the pyriformis muscle above to the upper apex of the popliteal space below. It is of no importance if the bifurcation of this nerve takes place at a higher level than the lower third of the thigh. It is equally unimportant if in 15 per cent of cases the sciatic nerve does not exist technically because of failure of fusion between its two component parts, the internal popliteal or tibial nerve and the external popliteal or peroneal nerve. When these two nerves arise independently in the sacral plexus and pass through the posterior thigh as contiguous but separate structures, they still must be referred to as the great sciatic nerve while within the boundaries set above.

The sciatic nerve is surrounded by fatty tissue as it lies within a space between intermuscular septa. The lateral and medial walls of the space are composed of connective tissue, fascia. The two fascial walls partition members of the posterior muscle groups. In the upper portion of the thigh the vastus intermedius and the vastus lateralis occupy a lateral position, while the long head of the biceps femoris is medial. In the lower portion of the thigh the biceps femoris is lateral and the semitendinosus and the semimembranosus are medial. Under normal conditions the sciatic nerve moves freely within the space between the fascial walls of the intermuscular septa.

## PATHOLOGY

Inflammation of the fascial walls or of the cellular contents of the space between them results in the formation of fibrous connective tissue bands. These bands usually arise from the fascial walls of the space. If they arise from proliferation of the connective tissue stroma of the

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fatty tissue surrounding the nerve, they become adherent to the fascial walls. The bands are composed of dense fibrous tissue and usually cross the nerve trunk at right angles to its long axis. The bands are found most frequently in three locations: (1) at a point beneath the gluteal fold, (2) at the bifurcation of the nerve, and (3) at the upper limit of the popliteal space. Although these are the usual sites at which the bands are found, they may be present at any point along the course of the nerve. They may occur at a single site or at multiple points. The bands contract and press upon or constrict the nerve trunk. Secondary inflammation of the nerve sheath is frequently present as evidenced by congestion and hyperemia of the sheath beneath and above the constriction and by the presence of fine adhesions on the outer surface of the sheath.

The bands are often so strong that by hooking a finger beneath one the extremity can be lifted from the operating table without the band breaking or tearing.

#### CLINICAL FINDINGS

The chief symptom of the patients operated upon was severe pain localized to one sciatic nerve. The pain irradiated to the calf of the leg and frequently to the heel. The onset of pain was usually precipitous and most frequently followed exposure of the thigh affected to changes in temperature, the temperature change being from hot to cold. The pain was of such intensity that it could not be controlled except by opiates in large doses. The patients were confined to bed because of the pain. It was characteristic of the condition that, when in bed, a position for the affected extremity could be found which was pain free. Such position was found by the patient lying on the unaffected side; the affected thigh held in flexion, the leg flexed to 45 degrees, and the entire extremity supported in a position of moderate internal rotation and adduction by a soft pillow placed beneath the knee. Movement of the extremity from this position of rest caused immediate recurrence of the pain in all its severity. Palpation over the nerve increased the pain. At points along the course of the nerve the pain was more severe than elsewhere. These points of increased pain accorded with the sites of constricting bands.

The ankle jerk was absent. Atrophy of the calf muscles was present, the degree depending upon the duration of the disability. Hyperesthesia of the skin overlying the course of the nerve was present in all cases.

During the presence of pain, there was spasticity of the lower trunk muscles, especially on the affected side; relaxation of these muscles took place when pain was absent. Due to the severity of pain and the consequent loss of sleep, the morale of the patients was extremely low.

Not any of the patients had severe foci of infection. Abnormalities of the lumbar spine, lumbosacral joint, or the sacroiliac articulations were either absent or were found not to be responsible for the sciatic pain.

#### TECHNIQUE OF OPERATION

An incision was made on the posterior lateral aspect of the thigh from the gluteal fold to the popliteal space. The nerve was exposed by blunt dissection through the intermuscular septum between the biceps femoris and the semimembranosus and semitendinosus muscles. No muscles were cut. The sciatic nerve was examined and the presence of adhesions

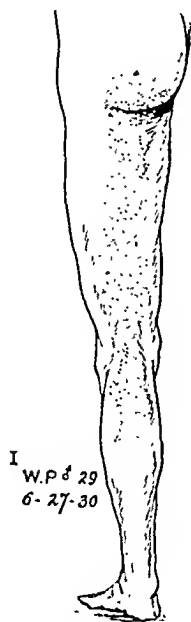


Fig. 1.

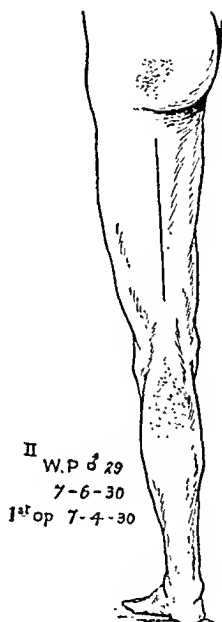


Fig. 2.

Fig. 1.—Case 9. The distribution of pain and skin hyperesthesia shown by stippling. Before operation.

Fig. 2.—Case 9. Residual pain following first operation at which several adhesions were removed from about the middle third of the sciatic nerve.

detected. The adhesions were freed by cutting. Great care was taken to prevent trauma to the nerve. The upper limits of the nerve were inspected by blunt dissection with the finger as high as the sciatic notch. The two popliteal nerves were followed by the finger well into the lower portion of the popliteal space. All bleeding points were ligated. The wound was closed in layers with interrupted sutures and usually without drainage.

The patients were kept in bed for from ten to fourteen days after operation. They were then allowed gradually to resume normal activity.



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The chief symptom of the patients operated upon was severe pain localized to one sciatic nerve. The pain irradiated to the calf of the leg and frequently to the heel. The onset of pain was usually precipitous and most frequently followed exposure of the thigh affected to changes in temperature, the temperature change being from hot to cold. The pain was of such intensity that it could not be controlled except by opiates in large doses. The patients were confined to bed because of the pain. It was characteristic of the condition that, when in bed, a position for the affected extremity could be found which was pain free. Such position was found by the patient lying on the unaffected side; the affected thigh held in flexion, the leg flexed to 45 degrees, and the entire extremity supported in a position of moderate internal rotation and adduction by a soft pillow placed beneath the knee. Movement of the extremity from this position of rest caused immediate recurrence of the pain in all its severity. Palpation over the nerve increased the pain. At points along the course of the nerve the pain was more severe than elsewhere. These points of increased pain accorded with the sites of constricting bands.

The ankle jerk was absent. Atrophy of the calf muscles was present, the degree depending upon the duration of the disability. Hyperesthesia of the skin overlying the course of the nerve was present in all cases.

During the presence of pain, there was spasticity of the lower trunk muscles, especially on the affected side; relaxation of these muscles took place when pain was absent. Due to the severity of pain and the consequent loss of sleep, the morale of the patients was extremely low.

It is emphasized that the 24 patients operated upon suffered from a specific type of sciatica. The pathology found at operation and the relief of pain which followed operation, proved the diagnosis to be correct in 23 cases.

#### CONCLUSIONS

The manner in which adhesions about the sciatic nerve produce local pain is analogous to the constricting action of the piriformis muscle as demonstrated by Freiberg.<sup>4</sup>

To give this form of sciatica a specific name is unnecessary; it is sufficient to recognize the fact that in some cases adhesions do form about the nerve and that when present they are responsible for the ensuing pain. When sciatic pain is due to the constriction of the nerve by adhesions, but one rational method of treatment is available, the sectioning of the adhesive bands by open operation.

#### SUMMARY

1. It is demonstrated that fibrous adhesions on occasion form about the sciatic nerve.
2. These bands press upon or constrict the nerve and produce sciatic nerve pain.
3. The pain so produced is of great intensity.
4. Complete relief from this pain can be obtained only by the operative exposure of the sciatic nerve throughout its course in the thigh and the removal of the constricting fibrous adhesions.

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## CASE DATA

The case group here reported is composed of 24 patients who suffered from unilateral sciatic pain. When first seen, the majority of the patients had been under treatment by other physicians for from three to ten weeks. During this time all the standard procedures for the relief of sciatic pain had been tried without benefit.

Upon the 24 patients, 28 operations were performed. Two patients were operated upon twice; 1 patient was operated upon three times. In 3 patients who failed to receive complete relief from pain following the first operation, it was found, upon subsequent operation, that all the

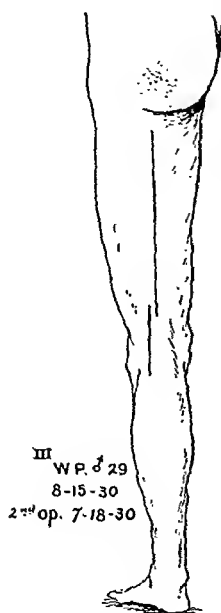


Fig. 3.

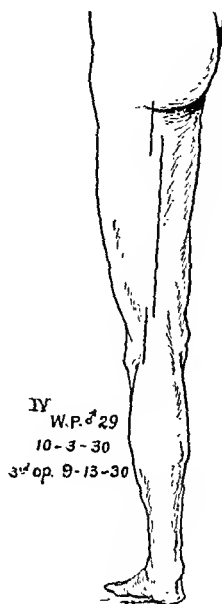


Fig. 4.

Fig. 3.—Case 9. Residual pain following second operation at which adhesions were removed from about the sciatic nerve in the popliteal space.

Fig. 4.—Case 9. Absence of all pain following third operation at which a large adhesion was removed from about the sciatic nerve in its proximal course. The patient has remained free from sciatic pain to date.

adhesions had not been freed. From these cases it was learned that the entire nerve must be exposed and examined carefully.

Of the 24 patients operated upon, 1 failed to receive any relief of pain. Two patients received but partial relief. The remaining cases were completely relieved of symptoms and have remained so for periods ranging from one to thirteen years. No complications developed following any of the operations. The patient who was not benefited by exposure of his sciatic nerve was operated upon some ten months later for a tumor of the cauda equina. The two patients who obtained but partial relief from pain refused subsequent operations.

## In Memoriam

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John Roberts Caulk

1881-1938

JOHN ROBERTS CAULK was born Oct. 30, 1881, at McDaniel, Md. He received his A.B. degree in 1901 and his M.A. in 1902 from St. John's College, Annapolis, Md. He attended Georgetown University 1901-1902 and graduated from Johns Hopkins University with an M.D. degree in 1906. From 1907 to 1910 he was assistant resident surgeon in the Department of Urology at Johns Hopkins Hospital. After finishing in 1910, he came to St. Louis and soon afterwards was appointed to the Department of Surgery of Washington University Medical School. Later, he became professor of Clinical Genito-Urinary Surgery in that institution and served in this capacity until the time of his death.

On June 1, 1910, he married Bessie Jenifer Harrison. Two children were born to them, John Roberts Caulk, Jr., and Elizabeth Caulk Evans. The former presented him with a grandchild, John Roberts Caulk, III, shortly before his death.

His staff appointments included most of the St. Louis hospitals. His membership in medical societies was unusually extensive. He was a F.A.C.S., member of the American Urological Association (of which he was president in 1925), Clinical Society of Genito-Urinary Surgeons, Southern Surgical Society, Missouri State Medical Society, St. Louis Medical Society, American Association of Clinical Genito-Urinary Surgeons (of which he was president in 1933), Southern Medical Association, and St. Louis Surgical Society (of which he was president at the time of his death in 1938).

He wrote many articles and published over a hundred in his comparatively short, active period of practice. His greatest scientific interest lay in furthering transurethral prostatic surgery, particularly by means of his cautery punch.

Everyone who met "Jack" Caulk, as he was most frequently known to his friends, appreciated that he had an outstanding personality with unusual geniality. His greatest ability lay in reflecting the mood of the person to whom he was talking. No one has ever seen John Caulk exhibit an ugly mood. He was always light, airy, and yet with indomitable will and untiring energy. His friends were legion over the United States, with many abroad. At the medical meetings following his demise, groups of men were earnestly requesting information of his sickness. He bore the trials of his sickness with the same great courage that he exhibited throughout his practice of surgery.

D. K. ROSE.



John Roberts Caulk  
1881-1938

ease of the liver at some time after its administration. There can be little doubt that arsenicals play an important role in the etiology of at least some of the hepatic cirrhosis which is seen so much more frequently in treated cases of syphilis.<sup>4</sup> It seems proper to ask whether the future incidence of cirrhosis of the liver will not be higher in individuals who previously have received intensive sulfanilamide therapy. The existence of this possibility should discourage at least the indiscriminate administration of sulfanilamide in cases where indications for its use are not clear cut.

As further evidence of the similar effects of arsenic and of sulfanilamide upon the liver, Garvin<sup>5</sup> has noted, among five instances of jaundice following administration of sulfanilamide, one in which temporary ascites occurred. Garvin recognized the fact that this has been observed from time to time in cases of arsphenamine icterus, as well as icterus due to other poisons.

According to recent studies of porphyrin excretion in the urine, sulfanilamide causes elaboration of coproporphyrin Type III<sup>6</sup> in common with other poisons, such as arsenic,<sup>7</sup> lead,<sup>8,9</sup> and probably mercury.<sup>10</sup> Although the significance of the formation of this porphyrin is not yet clear, it appears that its presence in the urine in any appreciable amount indicates a marked abnormality in pigment metabolism, and, so far as can be determined at present, one that is due to some type of poisoning. This is mentioned simply because it is another evidence of the fundamental changes which sulfanilamide may bring about and which require constant evaluation in the clinical use of this drug.

—C. J. Watson, M.D.  
Minneapolis, Minn.

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# Editorial

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## The Effect of Sulfanilamide Upon the Liver

It has been assumed often that the jaundice observed at times after administration of sulfanilamide is related closely to increased hemolysis or to actual hemolytic anemia. Recent study has brought the realization that liver damage, due to the drug, is the important factor in the appearance of jaundice. The cases reported by Bannick and his associates<sup>1</sup> indicated that fatal jaundice is much more likely to occur when the drug is given to individuals whose livers have already been damaged by pre-existing disease. In our experience jaundice has been noted to appear much more frequently in the individuals who are most sick at the time the drug is started. Three patients have been observed recently who were very ill, but not jaundiced, prior to administration of sulfanilamide. Jaundice appeared within forty-eight hours after the drug was given and in each instance disappeared within four days after its discontinuance. Two of these patients, suffering respectively from staphylococcus osteomyelitis and from peritonitis following roentgen therapy for cancer of the cervix, recovered satisfactorily from the acute phases of their disease; the third, an instance of beta hemolytic streptococcus empyema, has improved considerably but is still under observation. The sequence of events in these cases suggested strongly that jaundice was due to a summation of the effects of sulfanilamide and pre-existing liver damage.

Opinion has not yet crystallized as to whether the presence of jaundice or its appearance contraindicates the use or the continued administration of sulfanilamide. Long and Bliss<sup>2</sup> "do not believe that the previous existence of liver damage or jaundice is necessarily a contraindication to sulfanilamide therapy." On the other hand, Lockwood, Cohn, and Stokinger<sup>3</sup> regard jaundice as "an extremely disturbing development; in view of the possibility of permanent damage to the liver, sulfanilamide was discontinued whenever it appeared." This is undoubtedly the safest attitude, although the question of whether to discontinue the drug will have to remain a matter of judgment in each instance. The knowledge that sulfanilamide often damages the liver at least mildly makes it clear that the drug should not be given except where clearly indicated from an etiologic standpoint. In our experience moderate to marked increases of urobilinogen in the urine have appeared in the majority of individuals receiving sulfanilamide, even though they were not jaundiced. This is evidence of at least a temporary liver dysfunction.

A comparison of sulfanilamide with other drugs known to cause liver damage brings up the question of whether sulfanilamide may cause dis-

lable by other means. Thus, heparin is claimed to increase the resistance of erythrocytes to hypotonic salt solutions,<sup>82</sup> inhibit glycolysis,<sup>166</sup> increase the activity of herbivorous, but not human, phagocytes in the phagocytic index test for *Brucella* infection,<sup>83</sup> and to alter the sedimentation rate. In addition, all reactions involving complement may be affected because of the inhibitory action on complement mid-piece.

The value of sedimentation rates measured with heparinized blood has been the source of some discussion. On *a priori* grounds heparin would seem preferable to citrate or oxalate in that it avoids changes in the erythrocytes due to osmotic action, maintaining the blood in a more nearly physiologic state. In support of this, Plass and Rourke, who introduced the use of heparin in the sedimentation test,<sup>84</sup> found the sedimentation rates of hemophilic blood with and without heparin to be identical.<sup>85</sup>

The values obtained with heparinized blood differ considerably from those obtained when other anticoagulants are used,<sup>86</sup> on the whole being greater<sup>85, 87</sup> particularly in pathologic blood,<sup>88</sup> so that were heparin to come into general use, considerably different standards of rate would obtain for various conditions. Ström,<sup>86</sup> in a critical investigation and discussion, asserts that heparin is unsatisfactory, the error in duplicate tests being much larger than with citrate, and the rate in a given test showing surprisingly large and unpredictable fluctuations within the usual time of observation. In his experience, heparin added to citrate also alters the sedimentation velocity so that it is considerably different from that with heparin or citrate alone. It seems evident that controversy over the advantages and disadvantages of employing heparin in this test will continue for some time. In an interesting communication Zirm and Schenk<sup>89</sup> state that acceleration of the sedimentation rate when heparin is used may be observed during a considerable interval after the acute manifestations of various types of infection have subsided, at which time the rate by the conventional methods has returned to normal.

The inhibitory action of heparin on complement was first noted by Fuchs and Hartmann,<sup>49</sup> the effect being exerted upon the mid-piece which Fuchs and his collaborators believe to be identical with prothrombin. The observations supporting this claim and other literature on the subject have been dealt with in detail by Fuchs.<sup>18</sup> The complement inhibiting effect has been confirmed by a number of workers, and Wising<sup>90</sup> finds that with pure heparin the effect is observed at about the same dilutions as those capable of causing a minimal effect on coagulation. The identity of complement mid-piece and prothrombin is still a matter of controversy. Thus, Wising<sup>91</sup> has shown that treatment of heparinized serum with toluidine blue, which precipitates heparin quantitatively, does not liberate any complementary



# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## HEPARIN: A REVIEW OF ITS HISTORY, CHEMISTRY, PHYSIOLOGY AND CLINICAL APPLICATIONS

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(Continued from the March issue)

### PHYSIOLOGIC ASPECTS OF HEPARIN

*Heparin as the Physiologic Anticoagulant.*—This phase of the heparin problem has already been discussed in the sections on the chemistry and mechanism of heparin action. It will suffice to reiterate here that a mass of evidence has accumulated which sustains the concept that heparin is the product of certain specialized cells occurring in a wide variety of species and that it eventually enters the blood stream where it acts as the physiologic anticoagulant.

*Heparin as an Anticoagulant for Blood Specimens.*—The suitability of heparinized blood for various laboratory examinations has been extensively investigated. Crude or partially purified heparin did not modify any of the constituents ordinarily concerned in chemical analyses,<sup>5, 74, 75</sup> although in some preparations there has been sufficient calcium<sup>76-78</sup> and inorganic phosphorus<sup>77</sup> to introduce large errors into determinations of these when generous amounts of heparin were employed. Low values for calcium have also been reported,<sup>77, 79</sup> presumably due to the ability of heparin to form poorly dissociated salts.

"Pure" heparin or its salts are effective in such small quantities that no errors of this sort result from their use. Wilander<sup>80</sup> has reported that sugar, calcium, uric acid, nonprotein nitrogen, phosphatase, and hemoglobin are unaffected by heparinization. The red and white cell counts are unaltered, although the latter must be made rather soon after the blood is withdrawn in order to escape errors due to agglutination. An important use of heparin is found in making hematocrit determinations without disturbing the osmotic equilibrium between cells and plasma. Rather large amounts (8 to 10 mg. per 100 c.c. of ordinary commercial heparin) should be employed in order to obtain opaque cell layers with brief high-speed centrifugalization.<sup>81</sup>

Of the various other laboratory tests there are several in which heparinized blood behaves differently from blood rendered incoagu-

not be satisfactorily achieved in this manner in large animals. Nevertheless, considerable advances have been made by these workers in modifying heparin so that it is more suitable for subcutaneous injection. Considering the effects of protamine-insulin in prolonging the effects of insulin, they attempted to similarly alter heparin. The protamine derivative is insoluble<sup>24</sup> and forms a suspension difficult to inject; on the other hand benzidine forms a salt with heparin which is suitable for this purpose and is slowly absorbed, and with this preparation the effects of one large subcutaneous injection have been prolonged for as much as forty hours. The possible toxicity of benzidine is mentioned, but not discussed.

Observations on rats yielded similar results, although in some instances fatal hemorrhages occurred at the site of injection. It was concluded that the subcutaneous injection of pure or "modified" heparin was to be preferred in small animals, whereas constant intravenous injection is best where prolonged effects are desired in larger species.

The observations of Chargaff<sup>24</sup> on protamine-heparin were extended. The heparin present in a given sample of blood may be titrated by determining the amount of protamine necessary to alter the anti-coagulant effect to a given degree, as these substances apparently combine stoichiometrically, one milligram of protamine neutralizing 0.3 mg. heparin in vitro or in vivo. Protamine is toxic if administered in any form intravenously.

Jaques<sup>24</sup> studied the duration of heparin effects and its disappearance from the blood of dogs, and has pointed out some important principles. The maximum rate at which injected heparin (pure) disappears is of the order of 2 units (0.02 mg.) per kilogram per minute, a further increase in injection rate above this level leading to a progressive accumulation of heparin in the blood. At somewhat lower rates of injection the removal is proportional to the blood heparin concentration; however the effect on the coagulation time varies in individual animals in relation to their clotting factors. As there is no difference in the potency of heparin in vivo and in vitro the concentration of blood heparin necessary to establish a given coagulation time is readily determined, and from this and data on the rate of injection to blood heparin level, the rate required to set the coagulation time at any desired level is calculated.

It is generally agreed that there is no "negative phase" in the coagulation time as the effects of administered heparin wear off, i.e., the blood does not become temporarily hypercoagulable.

*Heparin and Experimental Thrombosis.*—The value of heparin as an agent in the study and prevention of thrombosis was appreciated by Howell. The initial report of its experimental use in this respect is that of Mason,<sup>25</sup> who found that the course of intravascular clotting

properties. The validity of argument from this rests upon the assumption that heparin inactivates prothrombin; on the other hand one of the arguments for the identity of complement mid-piece and prothrombin is heparin inhibition of the former.

*The Effects of Intravenous and Subcutaneous Administration of Heparin to Experimental Animals.*—Single doses of crude heparin<sup>4</sup> and multiple doses of partially purified heparin<sup>92</sup> were administered intravenously to dogs by Howell without any deleterious effects. Reed, likewise, did not find crude heparin toxic.<sup>5</sup> However, the experience of many with the partially purified commercial preparations seems to have been like that of the writer, viz., some lots of heparin seemed to be tolerated quite satisfactorily by most experimental animals, whereas others brought about reactions of varying degrees of severity, attended by fall in blood pressure, weakness, collapse, rise in temperature, retching and vomiting, and occasionally death if large doses were employed. An occasional animal manifested a toxic response to preparations most other animals tolerated well. Autopsy findings in such cases are reported by Murray et al.<sup>93</sup> The dosage of these heparin preparations required to produce a given extension of coagulation time in vivo or in vitro varied markedly with the preparation. There is universal agreement that highly purified heparin having an activity of the order of 500 Howell cat units per milligram may be injected in large quantities without untoward effects of any kind, and that the toxicity of the older, weaker products is due to contaminants, not to heparin itself.

The administration of purified heparin has been discussed by Jaques, Charles, and Best<sup>23</sup> in the case of dogs and rats. A given dose raised the clotting time to a variable degree in different dogs, e.g., 35 units (0.35 mg.) per kilogram of body weight raised the clotting time from the normal three minutes to a period of from fifteen minutes to greater than one and one-half hours. The effects of such a dose wore off in about an hour. These authors find the most satisfactory method of administration for prolonged effects is by intravenous drip allowing continuous injection. After an initial single injection of 35 units (0.35 mg.) per kilogram a continuous injection of 25 units (0.25 mg.) per kilogram per hour is made, this rate being altered to obtain the desired level in clotting time according to observations on the individual animal.

When purified heparin is administered *subcutaneously* the effects depend on the dose and whether an anesthetic is employed or not. With large doses, e.g., 450 units (4.5 mg.) per kilogram in the presence of an anesthetic (nembutal), the clotting time was raised for ten to twelve hours; in the absence of the anesthetic the effects were much briefer. With smaller doses, 100 to 250 units (1 to 2.5 mg.) per kg., little effect was observed. The regulation of the level of clotting time can-

the infusion of heparin into a vein or artery at such a rate that the coagulation time of the general circulation is increased more or less equally in all localities.

In a later paper, Murray and Best<sup>101</sup> reported the results of employment of regional heparinization in blood vessel surgery in dogs. The percentage successes in arterial anastomoses was markedly increased, and when the lumen was kept patent seventy-two hours, the suture lines were healed. Grafting of a section of vein between the ends of a sectioned artery was also accomplished. Recurrence of arterial emboli after removal of the initial one was diminished by either regional or general heparinization, and mechanical injury to the splenic vein was not followed by thrombosis in the portal system when heparin was used. Transplantation of organs was also greatly facilitated. The clinical observations of these investigators will be mentioned later.

The study of thrombosis produced by chemical injury has been extended by Solandt and Best<sup>102</sup> to studies of this process in the coronary artery of dogs. A small section of the left branch is freed from the myocardium, pinched off with clips, and injected with sodium ricinoleate, a procedure which regularly leads to subsequent development of occlusion after the clips are removed and the circulation restored. General heparinization initiated prior to injection of the ricinoleate, continued for twelve to twenty-four hours, prevented thrombus formation in the damaged artery during that time. Prolonged therapy designed to give the intima a chance to heal had not been undertaken at the time of this report. The clinical possibilities these experiments suggest are hampered by the absence of adequate premonitory signs of onset of an acute coronary crisis.

The contributions of the Toronto group to the various phases of the heparin problem have been summarized in an interesting lecture by Professor Best.<sup>103</sup>

The value of heparin in a large variety of circulatory disorders will no doubt be reported in the future. Thus, for example, it apparently does not modify the vascular sequelae of experimental frostbite produced by localized exposure to cold, in the case of cats.<sup>104</sup>

*Heparin and Experimental Pleurisy.*—Widström and Wilander<sup>105</sup> have reported benefits from the use of heparin in experimental pleurisy produced in rabbits by injection of a dilute iodine solution into the right pleura, followed by multiple injections of 10 mg. of heparin starting five to six hours later. In control animals a copious exudate was formed which became interwoven with a fibrin net, the fluid being gradually adsorbed leaving a partially organized fibrin residue, the lungs being adherent in places. In those animals receiving heparin no fibrin appeared in the exudate and although this was more sanguineous, absorption was very rapid, and no adhesions were found. Heparin

produced by injection of extracts of lung (thromboplastic substance) into dogs and rabbits could be modified by previous injection of heparin, and when sufficient amounts were used no embolism resulted. Shionoya<sup>96-98</sup> studied the influence of crude heparin on extracorporeal thrombosis, i.e., the development of thrombi in a collodion tube through which an arteriovenous shunt was established between the carotid and jugular vessels in rabbits, a method permitting careful visual inspection of the growing thrombi. He found that whereas red thrombus formation was retarded by heparinization, white thrombi (platelets and leucocytes) deposited on the walls of the foreign surfaces, increasing downstream, although the appearance of fibrin shreds in and around them was delayed. The deposition of white thrombi was prevented by a combination of heparin and magnesium sulfate, but the toxicity of the latter rendered its therapeutic value doubtful.<sup>98</sup> It was the opinion of Professor Howell, at the time, that pure heparin alone would be found to prevent white thrombi accumulation,<sup>96</sup> which was found to be the case by Best, Cowan, and MacLean<sup>99</sup> in similar extracorporeal loop experiments on dogs, in which the purified heparin of Charles and Scott was employed, and in later experiments, this was also found to be true in the case of cats and monkeys, and to a lesser extent, in rabbits.<sup>100</sup> The extension from the primary mass was downstream.

The Toronto workers have also studied the effect of heparin on thrombosis following mechanical and chemical injury to veins in dogs.<sup>93</sup> Mechanical injury was produced by crushing an exposed vein followed by repair of the superficial wound if the experiment was prolonged. Heparin was administered intravenously just before the vein was damaged. Their findings indicated that heparinization prevented, in most instances, the immediate occlusion of the vein following injury, but that thrombus formation occurred when the effect of the heparin wore off. On the other hand, if continuous intravenous injection of heparin was undertaken so that the clotting time was raised until the intima healed, the incidence of occlusion was diminished markedly. For the type of injury they produced, heparinization was required for about three days. Similar results were obtained in experiments involving chemical injury to veins by ricinoleate, except that in these cases heparin was less effective when extensive injury was produced by strong solutions. With lesser degrees of injury the results were extremely good. The authors introduced certain descriptive terms to indicate the manner of administering heparin. "Local heparinization" refers to application of heparin to one particular area. "Regional heparinization" means the administration of heparin so that the circulating blood in one part of the body is rendered relatively less coagulable than that of other parts, e.g., by judicious intra-arterial injection. "General heparinization" describes

the infusion of heparin into a vein or artery at such a rate that the coagulation time of the general circulation is increased more or less equally in all localities.

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alone did not damage the normal pleura. It should be remembered that heparin is nondialyzable and thus exerts a prolonged effect.

*Heparin and Exchange Transfusion.*—The term "exchange transfusion" has been applied to the techniques in which the blood of the donor and that of the recipient are exchanged either by cross circulation or by cross injections and withdrawals of blood, the usual purpose being to allow the kidneys of the normal recipient to clear the metabolic end products from the blood of a donor with renal insufficiency. Efforts to do this without the aid of an efficient anticoagulant are complicated by the appearance of thrombi.<sup>106</sup>

The use of purified heparin in such experiments was first made by Thalhimer<sup>107</sup> in making cross injections and withdrawals of blood between normal (anesthetized) and bilaterally nephrectomized dogs in order to relieve the developing uremia in the latter. In a later paper Thalhimer, Solandt, and Best<sup>108</sup> report further experiments in which the exchange of blood between donor and recipient is continuous and regulated by a special pump<sup>109</sup> designed to deliver exactly equal quantities of blood in two directions, and permitting as much as 12 L. of blood per hour to be exchanged between dogs weighing about 8 kg., one of which had been previously bilaterally nephrectomized. In experiments of long duration, made possible by adequate use of purified heparin, the blood and tissues of the two dogs came to equilibrium in respect to urea, followed by a rapid fall of urea in the mixed bloods as urinary excretion progressed in the donor animal, the uremic partner losing those symptoms referable to nitrogen retention. Autopsies failed to reveal any damage of the organs of either animal. It was noted that occasional difficulties were encountered because of blood incompatibility between the dogs. Although dogs do not have definite blood groups, some possess isoagglutinins and hemolysins which agglutinate and hemolyze the red cells of other dogs, a complicating factor which has often been ignored in experimentation on this species.

Thalhimer<sup>107</sup> also reported experiments in which the heparinized blood of the nephrectomized dog was led through an extracorporeal loop consisting of cellophane sausage casing so arranged to permit continuous dialysis against saline as a means of removing the accumulated end products, a procedure which has been described in slightly modified forms by others, beginning with Abel in 1913.<sup>107</sup>

*Heparin and Anaphylactic Shock.*—In 1926 Kyes and Strauser<sup>110</sup> published experiments showing that anaphylactic shock produced in pigeons sensitized to sheep serum was obviated if, just prior to the injection of the critical dose of antigen, sufficient heparin was administered intravenously to render the blood incoagulable. The results were entirely convincing and were interpreted as supporting the hypothesis that in the acute stage of anaphylaxis there is widespread intravascular fibrin formation with resultant generalized embolism of

minute peripheral vessels. Heparin was presumed to inhibit this fibrin formation. Although anaphylaxis is accompanied by prolonged clotting time,<sup>111</sup> it had been shown<sup>112</sup> and confirmed<sup>113, 114</sup> that this prolongation is preceded by a brief period during which the blood is hypercoagulable. The obvious importance of these observations led to similar studies by several investigators. The results in each case are almost equally convincing, but most contradictory. Confirming the Kyes-Strauser claim are the results of Williams and van de Carr<sup>114, 115</sup> and Doxiades and Lemke<sup>116</sup> on guinea pigs sensitized to horse serum. The work of Mills<sup>117</sup> is only indirectly supportive in that he found that rendering the blood of guinea pigs sensitized to egg white hypercoagulable by injection of tissue extracts exaggerated the response to the subsequently injected antigen.

On the other hand, the beneficial effect of heparin was not confirmed by Hanzlik, Butt, and Stockton<sup>118</sup> with pigeons sensitized to horse serum, nor by Reed and Lamson,<sup>119</sup> Hyde,<sup>119</sup> Loewenthal,<sup>120</sup> Bradley and Dragstedt<sup>121</sup> and Klopstock<sup>122</sup> with guinea pigs similarly sensitized. Waud<sup>123</sup> and Reed<sup>124</sup> believed that heparin increased the severity of the anaphylactic responses they observed. It may be stated, therefore, that while anaphylaxis may occasionally be ameliorated under certain conditions by heparinization, there is no evidence that this is generally so, nor can the evidence be taken to support the contention that acute anaphylactic shock is associated with intravascular fibrin formation.

The prolongation of clotting time accompanying anaphylaxis is associated with an increase in blood heparin<sup>125</sup> and this may be titrated with protamine. When a hepatectomized dog is thrown into anaphylactic shock there is no increase in clotting time and the blood heparin is not altered, indicating that the liver is the source of the anticoagulant liberated during anaphylaxis.

The clotting time and blood heparin are also increased in peptone shock, as was shown by Howell<sup>7</sup> and confirmed by the protamine titration.<sup>125</sup>

The injection of homologous or heterologous tissue extracts may cause widespread intravascular coagulation in the recipient, an effect of the thromboplastic material in these extracts, and not related to sensitization phenomena. These consequences may be avoided by preliminary heparinization as has been shown by Mason<sup>95</sup> and Roome and Wilson.<sup>126</sup>

*Heparin and Tissue Culture.*—Cracium<sup>127</sup> first called attention to the advantages of heparinized plasma as a stock medium for tissue culture; however, observations such as those of Goerner,<sup>128</sup> who found exposure of Flexner-Jobling rat sarcoma tissue to heparin-inhibited subsequent growth, indicated that specific effects of heparin might



have to be considered. Fischer and Parker,<sup>129</sup> in study of growth and differentiation, employed heparin in certain experiments in which proliferation was depressed and differentiation enhanced, a result which Zakrzewski<sup>130</sup> showed to be referable to the inhibitory action of heparin on growth of cultures under these conditions. The addition of prothrombin to the culture medium stimulated proliferation; addition of heparin inhibited this and permitted differentiation. He regarded prothrombin as a stimulator of cell proliferation which could be inhibited by heparin, thus indirectly causing differentiation.<sup>131</sup> Later<sup>132, 133</sup> he found that Jansen sarcoma cells cultured by the Fischer-Parker method in serum had their growth inhibited when heparin plasma was added, as was the case for normal cells. The latter regularly differentiated in spite of growth standstill, whereas the sarcoma cells did not differentiate and resumed their rapid growth even after two months' inhibition, when returned to an optimal growth environment. Similar effects could be obtained with additions of heparin to serum, showing a fundamental difference in the behavior of normal and tumor tissue. Serum alone is not suitable for long time culture of normal tissue; however, addition of heparin inhibits growth to an extent that this otherwise insufficient medium will support its needs, under which conditions differentiation occurs.<sup>134</sup> Other anticoagulants behave similarly, and as heparin and prothrombin both occur physiologically, Zakrzewski believes they are probably of great importance in growth and regeneration processes. Inhibition of growth by heparin has also been observed in the case of yeast.<sup>135</sup>

*Heparin and the Reticulo-Endothelial System.*—Von Jancsó<sup>136</sup> has employed heparin in experiments designed to study the mechanism of reticulo-endothelial blockade by colloidal metals. He has shown that the storage of these foreign substances by reticulo-endothelial cells takes place in two phases: (1) adsorption on the surface of the cell facilitated by the previous formation of a fibrin network around the particle, and (2) vacuolar storage of the adsorbed particle in the cell. The preliminary process, therefore, resembles that of coagulation, and is inhibited by heparin (and several other anticoagulants). A specific means, therefore, is available for blocking this type of behavior of these cells without poisoning or in any other way diminishing their potential activity.

*Heparin in Experimental Obstructive Jaundice.*—The observations of Hillman et al.<sup>137</sup> indicate that in experimental obstructive jaundice in dogs, the blood heparin is not increased, as determined according to Howell's method, and cannot be responsible for the increase in coagulation time. Similar conclusions are drawn by Chergaff<sup>21</sup> who failed to reduce the clotting time in such instances by addition of protamine which combines with and destroys the effect of heparin present in blood.

*Bactericidal Action of Heparin.*—Heparin does not inhibit the growth of staphylococci in blood in vitro,<sup>138</sup> nor does it lessen the mortality of dogs with staphylococcus bacteremia when injected intravenously.<sup>139</sup>

*Metabolism of Heparin.*—The apparent physiologic sources of heparin have been discussed in the section on chemistry. Respecting the fate of heparin reaching the blood stream physiologically or in consequence of administration, very little seems to be known. In the case of a dog given multiple injections of partially purified heparin, Howell<sup>92</sup> was able to recover from the urine a portion of that injected. Jaques,<sup>94</sup> on the other hand, found only traces in the urine and feces, but was able to extract increased amounts from the intestines of heparinized dogs. Yankovsky<sup>140</sup> reported that in rabbits the rate at which heparin disappeared from the blood was not influenced by bilateral ligation of all renal vessels, but that when the intestines, spleen, stomach, and pancreas were removed, and the renal vessels ligated, the action of heparin was markedly prolonged. It has been shown, however, that heparin is rapidly inactivated by serum in vitro, particularly when warmed,<sup>69</sup> and this phenomenon is probably in part responsible for the rapid "disappearance" of heparin from the blood when the coagulation test is used for its assay. The reactions heparin has been shown to undergo with protamine and toluidine blue afford methods by which the fate of this substance may be more adequately studied in the future.

#### CLINICAL ASPECTS OF HEPARIN

*Standardization of Units.*—The lack of a uniform standard of potency for heparin preparations is a source of confusion in the literature. A number of "units" are found, the comparative value of which must be traced through the original literature. Recent trends are toward the use of either of the following standards: (1) the original Howell unit, which is that activity which keeps 1 c.c. of cold cat's blood fluid for twenty-four hours; (2) the unit of the Toronto workers, which is the activity of  $\frac{1}{100}$  mg. of the crystalline barium salt of purified heparin<sup>141</sup> and which is about five times as large as the Howell unit; and (3) expression as simply the weight of heparin employed. In the latter instance it is to be remembered that purified heparin preparations differ in potency, although one is not seriously in error in considering the pure substance to have an activity of about 500 Howell cat units per milligram.

*Effects of Intravenous and Subcutaneous Injections.*—The first observations on the effects of intravenously injected heparin in man were made by Howell<sup>8</sup> who found the preparation he used fairly well tolerated; however the experiences of others with partially purified commercial preparations or products isolated by Howell's or other methods indicated that these were unsuitable for clinical use,<sup>142, 143</sup> often pro-

ducing headache, chills, fever, fall of blood pressure, and other undesirable reactions. These were traceable to contaminants rather than to heparin itself, as pure preparations have been shown to be non-toxic and may be administered in large doses with safety.

The first clinical report in this respect is that of Hedenius and Wilander,<sup>144</sup> who studied the effects of single and multiple injections on the coagulation time, and various other functions in seventeen patients. No changes were observed in temperature, blood pressure, red cell count or fragility, white cell count and differential or sedimentation rate. There were no unpleasant subjective symptoms. The effect upon the coagulation time depended upon the dose given, 20 mg. increasing it to ten minutes within ten minutes after administration, whereas 60 mg. increased it to 30 minutes after the same interval. The effects rapidly wore off, the coagulation time returning to normal within an hour after 20 mg. and three hours after 60 mg. Doses between these exhibited proportionate effects. The normal coagulation time by the method employed<sup>145</sup> is five to seven minutes. Multiple injections prolonged the effects. The findings of Hedenius and Wilander have been confirmed by others who have made similar tests of heparin effects prior to its use in transfusions (*vide infra*). Best and his co-workers have also made observations on the effect of single doses<sup>93</sup> but prefer to establish heparinization by continuous intravenous drip by which the coagulation time may be maintained at any desired level for lengths of time, which in their cases have reached fourteen days.<sup>141</sup> The dosage varies considerably with the individual, and the coagulation time must be observed and the inflow of heparin adjusted accordingly. Thus to keep the clotting time at three times its normal value they employ a saline solution containing 1,000 units (10 mg.) heparin per 100 c.c. and allow this to run into the vein at the rate of about twenty-five drops per minute, changing the rate in accordance with the measured effect on the coagulation time.<sup>141</sup>

Heparin is effective when administered subcutaneously, as has been shown in animal experiments. No systematic study of the effects of subcutaneous injections on patients has been reported. Presumably, the objections met with in the animal experiments would be encountered clinically. It is ineffective orally.

*Heparin and Blood Transfusion.*—The possibilities of heparin as an antieoagulant for facilitating blood transfusions were recognized by Howell, who used it in several instances as early as 1928.<sup>5</sup> The results were fairly satisfactory; however, other investigators who employed the partially purified commercial preparations found that the danger of untoward reactions was too great to warrant its substitution for citrate.<sup>142</sup> Preparations varied in toxicity but did not display antigenic properties.<sup>146</sup>

The production of "pure" heparin reawakened interest in this phase of its use. The preparations purified by the means considered in the section on chemistry appear to be nontoxic and are tolerated intravenously by man in large quantities without any change in pulse rate, blood pressure, respiratory rate, blood chemistry, or numerous other functions which have been investigated other than coagulation and bleeding time, sedimentation velocity, fragility, and reactions involving complement (*vide supra*). Of these the significant effects are the prolongation of the clotting and bleeding time to an extent dependent upon the dose employed. A large number of reports have accumulated, all of which indicate that toxicity is no longer a factor militating against administration of heparin to man. The injected heparin solution, of course, must be sterilized, and fortunately this may be done without in any way damaging its anticoagulant activity by either boiling, or preferably, autoclaving at 110° C. for half an hour. Autoclaving for longer periods or at higher temperatures leads to inactivation, presumably by hydrolysis of the sulfate esters or depolymerization. Bacterial filters cannot be used because of adsorption of the heparin by the filter wall.<sup>45</sup> Sterile heparin in solution may be preserved in ampoules indefinitely without loss of potency.

The transfusion methods in which heparin has been employed fall into three general categories: (1) direct methods in which heparin solution is used to dampen the foreign surfaces of syringes, rubber connecting tubing, etc., to delay clotting thereon, (2) indirect methods in which it substitutes for citrate, and (3) either direct or indirect procedures in which the donor is heparinized prior to operation, so that the blood withdrawn is incoagulable for a suitable period. The heparin preparations used, for the most part, have been of four kinds: (1) that purified by Jorpes' method and obtained from the Carolyn Institute, Stockholm, (2) "Vetren," a heparin solution marketed by Promonta Chemisches Fabrik, Hamburg, (3) heparin purified by the methods of Charles and Scott, and available from the Connaught Laboratories, Toronto, and (4) pure heparin solution supplied by Hoffmann-La Roche, Basel, Switzerland.

The first report of the extensive use of purified heparin in blood transfusions is that of Skold<sup>147</sup> who used the Jeanbreaux indirect technique in which heparin was substituted for citrate in twenty-four instances. Jorpes' purified heparin, 0.5 per cent in 0.3 per cent tricesol was added to 20 to 25 c.c. of sterile saline in the receiving flask so as to give a heparin concentration of 4 to 5 mg. per 100 c.c. of blood, a dose large enough to give a considerable margin of safety against coagulation. In one instance some fibrin formed on the walls of the flask, and in another the recipient experienced a slight chill. It is necessary, of course, that the saline containing the heparin be thoroughly mixed with the blood by agitation; on the other hand foaming

ducing headache, chills, fever, fall of blood pressure, and other undesirable reactions. These were traceable to contaminants rather than to heparin itself, as pure preparations have been shown to be non-toxic and may be administered in large doses with safety.

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pense of the larger amounts of heparin required and the fact that the donor's coagulation time is raised for several hours after the injection. The latter objection does not appear to be one of any consequence. The procedure has been employed by others with success.<sup>151</sup>

The clinical experiences thus far reported appear to justify the conclusion that heparin is a useful adjunct in performing transfusions and permits simplification of the technique to the point that in the future it may be readily performed by the practicing physician in the patient's home.

*Heparin and Thrombosis.*—By far the most important possible clinical use of heparin is the prevention of postoperative thrombosis, yet little can be said concerning this at the present time. As Professor Best has pointed out, a large number of carefully controlled cases must be available from clinics where all the facilities necessary for the study are available, and where a fairly constant type of postoperative care is practiced before a certain evaluation may be made.<sup>141</sup> At the moment this may be said: In the results thus far obtained by animal experimentation, and in the limited clinical reports available there is nothing to indicate that heparin will not be therapeutically useful in this respect; on the other hand, all the evidence accrued supports the belief that it should be an extremely valuable weapon with which to combat thrombotic complications following various surgical procedures.

Heparin for this purpose is employed to render the blood less coagulable for a suitable time postoperatively to antagonize the thromboplastic substance entering the circulation during and following operation and until sufficient healing of cut surfaces has taken place to minimize thrombus formation at those points. It also prevents coagulation of stagnated blood in consequence of altered local or general circulatory dynamics. Progress in this phase of the problem may be summarized as follows: Heparin preparations suitable for long-continued administration without untoward reactions on the part of the patient are available. The range of dosage, mode of administration necessary to maintain the coagulation time at a suitably high level, and time following operation before heparin may be given without great risk of excessive bleeding, are fairly well established.

Concerning the dosage, there is some variation to be expected with the individual patient and with the particular heparin preparation employed. Very few figures on patients are available. For animal experiments (dogs), Best and his collaborators<sup>103</sup> employ an initial dose of 40 units per kilogram (= 0.4 mg. pure heparin of Charles and Scott per kilogram) and follow this by a continuous saline intravenous drip containing heparin at the rate of 30 units (0.3 mg.) per kilogram per hour, but somewhat lower dosages are used on patients.<sup>141</sup> For the time being the surgeon must regulate the dosage according to the observed clotting time of the individual subject. Crafoord<sup>153</sup> prefers

and splashing must be avoided in order to avoid formation of small shreds of fibrin, or frank clots, in consequence of interfacial adsorptive forces, independent of the type of anticoagulant present.

The usefulness of heparin employed in this manner has been adequately confirmed.<sup>148-151</sup> The amount entering the recipient is too small to seriously alter the coagulation time which may remain the same or be only slightly lengthened for an hour or two. This fortunate circumstance is apparently related to the "threshold" behavior of heparin in its effect upon coagulation time<sup>38</sup> and to the fact that it seems to be rather rapidly destroyed, excreted, stored, or inactivated after administration. Large excesses of tissue factor (thromboplastic substance, cephalin) overcome the action of heparin and it has been found safe, therefore, to employ it for transfusions immediately after or during surgical operations.<sup>148, 149</sup> A simplification of Clemens' apparatus<sup>148</sup> for indirect transfusion employing heparin has been described recently by Heim.<sup>150</sup> In this procedure the tubing surfaces are dampened with heparin solution before the blood is drawn into the receiving flask which also contains some of the solution.

In all these reports it is stated that no difficulties are encountered from either clots or untoward reactions by the recipient. The latter, when they occur, are traceable to sources other than the anticoagulant.<sup>148</sup> The quantities of heparin which should be used in these indirect procedures depend upon the particular preparation employed. Inasmuch as it is preferable to use too much rather than too little, 3 or 4 mg. of the highly purified heparin preparations per 100 c.c. of blood is to be recommended for the time being. Experience may justify a considerable reduction of this. Larger amounts are needed in case the blood is to be stored or kept for any length of time before administration to the recipient.

Hedenius<sup>152</sup> proposed the procedure of heparinizing the donor, the subsequent transfusions being performed by either direct or indirect methods. In his initial report eleven cases were considered, the dosage being 50 to 150 mg. of Jorpes' purified product. It was later decided that one milligram per kilogram body weight was the satisfactory dosage for donor heparinization.<sup>38</sup> The donor coagulation time ten minutes after injection is raised from the normal five to seven minutes to fifteen to thirty minutes, this being sufficient time to finish the transfusion routine. No untoward reactions occurred in either donor or recipient. It should be pointed out that this method requires only the simplest apparatus and minimum manipulation. It has the additional advantage of introducing a minimum amount of heparin into the recipient, and in Hedenius' cases the coagulation times were slightly shortened rather than lengthened. In opposition is the ex-

against Ringer solution and reinjected. Considerable amounts of non-protein nitrogen were removed in this manner during periods of dialysis as brief as half an hour. He found this technique easier to perform than that of creating an extra corporeal loop in which the dialyzing apparatus was part of the circuit. The clinical conditions in which this sort of treatment, or exchange transfusion, might be extremely useful include the reflex anurias, e.g., after operation on one kidney, postoperative renal insufficiency, anurias following insertion of indwelling catheters, or after suprapubic cystotomy preparatory to prostatectomy, anuria following severe burns, phenol intoxication, mercury poisoning, certain infections, etc. In these instances if terminal uremia can be avoided for a time, there is the possibility that an adequate degree of renal function may return. Exchange transfusion in which purified heparin is employed has not as yet been employed (reported) clinically.

*Heparin in Patients With Jaundice.*—The evidence from animal experiments<sup>137</sup> and the observation of Chargaff,<sup>24</sup> that addition of protamine to blood from patients with obstructive jaundice does not alter the coagulation time, make it probable that the increase in this function in such cases is not due to an increase in circulating heparin.

*Heparin and Hemophilia.*—Weil<sup>150</sup> in 1905 first suggested that the failure of hemophilic blood to clot was due to the presence of an excess of an antieoagulant, and in spite of evidence to the contrary this theory has been reiterated from time to time. Most recently Fuchs and von Falkenhausen<sup>160, 161</sup> have stated that an excess of antiprothrombin is to be found in the blood of patients with hemophilia. Howell had already reported heparin (antiprothrombin) to be present in normal quantities in this disease,<sup>162</sup> and in light of Fuchs' and Falkenhausen's report, Evans and Howell<sup>163</sup> repeated their work using their method.<sup>164</sup> The results, although only one patient was studied, showed conclusively that there was no excess heparin in hemophilic blood. It may be taken that whatever is the cause of hemophilia, it is unlikely to be associated with any disturbance in the level of blood heparin.

*Heparin and the Reticulo-Endothelial System.*—The interesting experiments of von Jancsó's<sup>136</sup> have been confirmed in the case of patients by Godlowski,<sup>143, 165</sup> who employed the Adler-Reimann Congo red test of reticulo-endothelial activity, and found that heparin inhibited the ability to take up the dye. This may become of interest as patients are submitted to longer intervals of heparinization.

*Heparin and Complement.*—It must be borne in mind in interpreting certain laboratory tests on heparinized patients that complement may be inhibited. This aspect seems not to have been studied as yet clinically.



multiple injections over continuous administration, and he finds it best to delay heparin administration until three hours after operation in order to avoid excessive bleeding, while Murray and Best<sup>101</sup> wait four to twenty-four hours, avoiding cases in which there is any doubt about oozing or bleeding. The criteria for cessation of heparin injection are stated by Murray and Best<sup>101</sup> as follows: ". . . when the patient has regained normal activity, i.e., when factors thought to contribute to the production of thrombosis have ceased to act. This time has been reached when shock has passed, and the blood pressure and circulation are normal; the incision has healed and is not painful, so that deep respirations are possible; the patient feels well and energetic and moves about actively in bed and can do exercises; distention is gone; the appetite has returned to normal; the chest is clear; and the temperature and pulse are normal." It is evident that this implies heparinization of considerable duration.

Bancroft, Stanley-Brown, and Chargaff<sup>154</sup> have discussed the evaluation of clotting tendencies in patients by various tests and the relation of these to the incidence of postoperative thrombosis. There is as yet no reliable means of accurately predicting which individuals present the greatest risk.

Murray and Best<sup>101</sup> also reported encouraging results in the employment of heparin following removal of peripheral arterial emboli to prevent recurrence during that time the intimal surfaces were healing, and in addition after splenectomy to prevent thrombosis in the portal vessels. None of 315 cases, of all kinds treated with heparin postoperatively, developed pulmonary embolism although many of the operative procedures were the kind in which this complication is relatively frequent. In their experience heparin was useful in treatment of phlebitis and pulmonary embolism, apparently preventing recurring embolism, and led to a more rapid improvement than that noted in a control group.

It is difficult to evaluate individual case reports in which heparin has been employed; however, favorable results have been noted in two cases of thrombosis of the central vein of the retina<sup>155, 156</sup> and in a case of thrombosis of the posterior-inferior cerebellar artery (Wallenberg syndrome).<sup>157</sup> Presumably, the benefits of the treatment result from more rapid resorption of hemorrhage, prevention of further coagulation at the site of hemorrhage, prevention of extension of the original thrombus, retraction and canalization followed by its slow removal by proteolytic enzymes.

*Heparin and "Blood Washing."*—Haas<sup>158</sup> has used partially purified heparin as an anticoagulant in his blood-washing technique in the treatment of uremia. The blood is removed by a syringe or cannula, and, after addition of heparin, placed in collodion tubes and dialyzed

against Ringer solution and reinjected. Considerable amounts of non-protein nitrogen were removed in this manner during periods of dialysis as brief as half an hour. He found this technique easier to perform than that of creating an extra corporeal loop in which the dialyzing apparatus was part of the circuit. The clinical conditions in which this sort of treatment, or exchange transfusion, might be extremely useful include the reflex anurias, e.g., after operation on one kidney, postoperative renal insufficiency, anurias following insertion of indwelling catheters, or after suprapubic cystotomy preparatory to prostatectomy, anuria following severe burns, phenol intoxication, mercury poisoning, certain infections, etc. In these instances if terminal uremia can be avoided for a time, there is the possibility that an adequate degree of renal function may return. Exchange transfusion in which purified heparin is employed has not as yet been employed (reported) clinically.

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It is clear that enormous strides have been made in the understanding of the chemistry and physiology of heparin, and that the purified product is now a useful clinical weapon from which much may be expected in the future. Nevertheless, a great deal remains to be learned, particularly respecting the physiology of this most interesting substance, and the present cost of the purified preparations (ranging from \$50 to \$100 per gram) must be reduced considerably before extensive clinical and laboratory studies may be undertaken in many laboratories and hospitals. Whether or not the production of a cheap synthetic and equally active analogue will be the solution of this economic problem remains for the future to disclose.

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It is clear that enormous strides have been made in the understanding of the chemistry and physiology of heparin, and that the purified product is now a useful clinical weapon from which much may be expected in the future. Nevertheless, a great deal remains to be learned, particularly respecting the physiology of this most interesting substance, and the present cost of the purified preparations (ranging from \$50 to \$100 per gram) must be reduced considerably before extensive clinical and laboratory studies may be undertaken in many laboratories and hospitals. Whether or not the production of a cheap synthetic and equally active analogue will be the solution of this economic problem remains for the future to disclose.

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bilateral fasciotomy was done. Dr. Green has treated 20 cases with 20 cures, although in 2 cases subsequent physiotherapy was necessary in order to give full relief. Some cases obtained immediate relief in the operating room. Moving pictures of 3 cases illustrated most satisfactory results.

Frank Dickson, Kansas City, Mo., in discussing this paper cited 87 fasciotomies, 50 of which were done for low back pain. He warned against the indiscriminate use of the procedure and gave criteria for selecting cases which might be relieved by fasciotomy, and he also referred to the importance of dividing the penetrating fibrous fasculi.

Willis C. Campbell and J. S. Speed, Memphis, Tenn., reporting their observations concerning the use of vitallium plates and screws in selected fracture cases, praised the work done by Dr. Venable which was presented before the Southern Surgical Association several years ago. The importance of careful skin preparation and operating room technique was stressed and the authors showed a new type of screw with threads extending all the way to the head of the screw. They find that removal of the plates usually is not necessary.

In discussing this paper, Charles S. Venable, San Antonio, Tex., agreed with Dr. Speed regarding the selection of cases, and, after expressing gratification over the confirmation of his observations regarding vitallium, he showed a vitallium cap which he has devised for use in hip arthroplasty. Edgar Gilcreest, San Francisco, Calif., considered the introduction of vitallium to be epoch-making, but warned against unnecessary employment of open reduction.

William D. Haggard, Nashville, Tenn., in a study of stones in the pancreas, reviewed the descriptions of pancreatic stones and brought the collected cases up to date with the addition of a new case. A total of 195 cases have been reported, 134 of which have been nonoperated cases. Etiology, symptomatology, associated conditions, age and sex incidence, and the factors concerned in precipitating attacks were considered. The value of x-ray examination in diagnosis was also discussed. Treatment, including consideration of the surgical approaches for removal of the calculi, was outlined.

In discussing the paper, Waltman Walters, Rochester, Minn., spoke about the improvement in methods of surgical approach to the pancreas and also emphasized the importance of "scout" x-rays. He suggested that diabetics have such x-ray examination to rule out pancreatic calculi.

John Staige Davis, Baltimore, Md., presented the theory and practical use of the Z-incision in the relaxation of scar contractures. The Z-incision was first described 80 years ago. Dr. Davis indicated the types of clinical lesions in which the Z-method can be advantageously employed and discussed the use of multiple Z's in some cases. Fifty to 100 per cent of the central line of the Z was the amount of effective lengthening secured. Softening and relaxation of skin by massage, in conjunction with use of the Z-plastic, was advocated. An important detail of the procedure is the necessity that the angles cut should not be greater than 60° or less than 20°. The procedure may be used to avoid grafting or shifting from a distant point, and he prefers it to skin grafting in cases where either procedure might be used.

J. Barrett Brown, St. Louis, Mo., in a presentation concerning the utilization of the temporal muscle and fascia in facial paralysis, gave the history of the method, which was first described by Blair. Besides demonstrating the method used, cases in which restoration of emotional expression had been attained were shown. The ultimate results in these cases depend, aside from the surgical procedure, on speech training and avoidance of overactivity on the sound side. The operation is advocated only when fifth nerve anastomosis is impossible.



# Review of Recent Meetings

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## REVIEW OF THE SOUTHERN SURGICAL ASSOCIATION MEETING, DEC. 6-8, 1938, WHITE SULPHUR SPRINGS, W. VA.

AMBROSE H. STORCK, M.D., NEW ORLEANS, LA.

*(From the Department of Surgery, School of Medicine, Tulane University)*

THE fifty-first annual meeting of the Southern Surgical Association was held in White Sulphur Springs, W. Va., at the Greenbrier Hotel, Dec. 6, 7, and 8. One hundred fifty-six members, including the senior members and honorary fellows, were present. Of forty papers on the program, thirty-seven were presented.

E. Dunbar Newell, Chattanooga, Tenn., expressed the belief that, because of recent advances in the management of gas bacillus infection, publications prior to 1934 are practically worthless for present clinical purposes. The low incidence of this type of infection observed in the Chattanooga area was discussed and the occurrence of gas gangrene in relation to varied types of trauma, including surgical operations, was presented. Dr. Newell emphasized the importance of very early diagnosis and he advocated the administration of prophylactic doses of antitoxin on three successive days for the purpose of reducing the virulence of the infection rather than as an absolute preventive. Débridement, accurate hemostasis, and the intravenous injection of 10,000 to 30,000 units of polyvalent antitoxin every eight hours were considered essential in the active treatment of gas bacillus infection. Sulfanilamide and x-ray therapy were also discussed. He believes that it makes little difference whether Dakin's solution, hydrogen peroxide, or potassium permanganate be used as an oxidizing agent. Dr. Newell presented a case of gunshot wound of the abdomen with gas bacillus infection which was successfully treated with 120,000 units of antitoxin, 10 gr. of sulfanilamide every four hours, hydrogen peroxide compresses, and x-ray therapy twice a day.

In discussing this paper, J. Duffy Hancock, Louisville, Ky., reported a case somewhat similar to the one reported by Dr. Newell which was treated in essentially the same manner. The patient was much improved within twenty-four hours and complete recovery followed. Ralph G. Carothers, Cincinnati, Ohio, disagreed concerning the value of x-ray therapy and thought that the favorable results following its use have been due to low virulence infections. In support of his opinion, Dr. Carothers referred to eight consecutive fatal cases treated at Cook County Hospital with x-ray. He considered decompression by means of fasciotomy a most important part of the treatment of gas bacillus infection. Grover C. Weil, Pittsburgh, Pa., discussed the recognition of gas bacillus infection by the detection of the sour-sweet odor emanating from the wound.

Charles C. Green, Houston, Tex., in considering back pain and pain along the sciatic nerve, reviewed the normal function of the iliotibial tract and indicated how division of this band can be done in order to relieve symptoms without producing undesirable collateral effects. The operative procedure was demonstrated by means of lantern slides, and several typical case reports were presented in which the procedure had been employed with favorable results, including one case in which

A. O. Singleton, Galveston, Tex., also discussed Dr. David's report and showed that in a statistical study of lymphogranuloma with rectal involvement in his service none had carcinoma. Harvey Stone, Baltimore, Md., asked whether Dr. Lahey would do a radical operation for a benign tumor in the hollow of the sacrum. He did not feel that the principle of preliminary colostomy should be applied in all cases. Fred W. Rankin, Lexington, Ky., in discussing Dr. Lahey's paper, also asked for clarification by Dr. Lahey regarding his indications for radical operation. In the past four years Dr. Rankin has done 87 one-stage, 25 two-stage, 6 two-stage modified Miles or Rankin operations. He expressed the belief that purgation and local irrigation in unobstructed cases can adequately prepare patients for a single stage operation. Alton Ochsner, New Orleans, La., commenting on the Devine colostomy, presented a method of avoiding the sacrifice of bowel between the clamps applied at the time of operation and he also advocated a transverse incision. He showed a modified Devine clamp devised by Michael DeBakey, New Orleans, La., which has a lighter superstructure, and he gave the results in 16 cases in which the Devine procedure was used. Dr. Lahey, in closing the discussion of his paper said that he did not do radical operations for benign lesions and added that he did not mean to advocate the Mikulicz operation in all cases as he sees no reason for not employing the one-stage operation in selected cases. He recommended that surgeons start with two-stage and change to one-stage operations as they become more proficient in resections of the large bowel.

Harvey B. Stone, Baltimore, Md., presented a method of surgical treatment for giant rectum and sigmoid. He reported two cases and described the successful treatment employed in one of these cases. In one case it was possible to regulate the bowels without surgical intervention. In the other case, a man who had had an imperforate anus and who had a stenotic opening, local plastic operations were inadequate, so laparotomy was done and the colon was mobilized, after which the patient was turned face down, the intestine around the anus was dissected, and then the bowel brought down and attached to the skin edges. Subsequent introduction of fascial strips to relieve incontinence was only partially successful. He believes that one case was of purely mechanical origin while in the other case there was no mechanical factor. Sympathectomy, he felt, would have done no good in either case. Carrington Williams, Richmond, Va., reported a case similar to Dr. Stone's second case; i.e., a 9-year-old patient who had had an imperforate anus. A colostomy was performed, followed by a fascial sling operation. Dr. Stone, in closing the discussion of his paper, said that he believed a colostomy alone would not have been sufficient in the case he reported.

John de J. Pemberton, Rochester, Minn., considered the anatomic factors of importance in the development of rectal prolapse and asserted that some abnormality of these structures must be present for development of prolapse. Dr. Pemberton reviewed five types of operations for prolapse, choice of which should depend on the condition existing in a specific case. All of the methods described have been intended to be curative, but in all instances there have been some recurrences. He cited reasons for failure of various types of operations, such as the one devised by Moschowitz. By means of lantern slides he showed a new method which he has employed in six cases.

Ambrose H. Storek, New Orleans, La., presented a résumé of intestinal obstruction due to intraluminal foreign bodies, notably gallstones, fecaliths, enteroliths,

Walter E. Dandy, Baltimore, Md., discussed this paper and expressed the belief that improved results are due to insertion of the fascia into the temporal muscle. He has used this method in several cases.

Vernon C. David, Chicago, Ill., in a paper entitled *The Relation of Chronic Inflammation and Especially Lymphogranuloma Inguinalis to the Development of Squamous Cell Carcinoma of the Rectum* discussed the incidence of the lesions as well as the occurrence of carcinoma in such lesions after varying periods of time. He recommended the employment of sulfanilamide in the treatment of lymphogranuloma inguinalis.

F. Webb Griffith, Asheville, N. C., reviewed the subject of primary carcinoma of the ileum and presented statistics in regard to the incidence of carcinoma of the small intestine. He then gave a case report in which a preoperative diagnosis of "probable carcinoma of the small intestine" was made. The absence of dependable diagnostic criteria was stressed.

R. H. Jackson, Madison, Wis., talked about the technique and demonstrable advantages of the Devine colostomy for defunctionalizing the colon. From his experience he considered it a distinct improvement over other methods for resection of the distal colon and one which has brought colectomy into a range of reasonable mortality. The merits of the method which he cited included: (1) benefits conferred upon the patient, consisting of control of the proximal meatus, maintenance of morale, ability to return home, and elimination of the necessity of isolation of the patient; (2) the benefits to relatives and friends; and (3) the benefits to the surgeon; i.e., a completely clean bowel, favorable position of the colostomy which affords a clean field below, and encouragement to perform resection and anastomosis at a lower level because the bowel is clean. General adoption of this method, he felt, should be accompanied by a decided lowering of mortality.

Frank H. Lahey, Boston, Mass., presenting deductions from 800 operations for carcinoma of the colon and rectum, emphasized the importance of rectal and colonic polyps. Seventy-five per cent of colon carcinoma is in the lower colon, rectum, and sigmoid, and he considers that many bowel carcinomas develop in polyps. He believes these lesions should be approached during the premalignant stage. Improved tables and other apparatus facilitate the care of these patients. He warned against fulgurating high polyps in one's office. In his cases malignant changes were observed at the tip rather than at the base of the polyp. He gave the percentages in which various types of operations have been done and cited the need for disseminating to the profession and the laity knowledge concerning colostomies in operable cases. Many cases do not require a colostomy bag. He mentioned the importance of seeing the patient after operation in order to give him confidence in his ability to manage the colostomy. Plastic procedures for scar-contracted colostomies were discussed.

In discussing Dr. Griffith's paper, John S. Horsley, Richmond, Va., presented a case of sympathicoblastoma, the histology of which had been variously interpreted by different pathologists. He additionally presented a chromaffin cell tumor. Curtice Rosser, Dallas, Tex., discussed Dr. David's paper and drew attention to the observation he made eight years ago concerning the relationship between inflammatory lesions and carcinoma. He deplored the fact that Kraske's opinion that such lesions as hemorrhoids, fissures, and fistulas bear no relation to carcinoma has been carried down in the literature and in the minds of medical men. Of his 16 cases of carcinoma arising from benign lesions, in 9 instances the growth was adenocarcinoma. He suggested that it was the fistula accompanying Dr. David's cases that incited the carcinoma, as he has never seen carcinoma develop in lymphogranuloma.

A. O. Singleton, Galveston, Tex., also discussed Dr. David's report and showed that in a statistical study of lymphogranuloma with rectal involvement in his service none had carcinoma. Harvey Stone, Baltimore, Md., asked whether Dr. Lahey would do a radical operation for a benign tumor in the hollow of the sacrum. He did not feel that the principle of preliminary colostomy should be applied in all cases. Fred W. Rankin, Lexington, Ky., in discussing Dr. Lahey's paper, also asked for clarification by Dr. Lahey regarding his indications for radical operation. In the past four years Dr. Rankin has done 87 one-stage, 25 two-stage, 6 two-stage modified Miles or Rankin operations. He expressed the belief that purgation and local irrigation in unobstructed cases can adequately prepare patients for a single stage operation. Alton Ochsner, New Orleans, La., commenting on the Devine colostomy, presented a method of avoiding the sacrifice of bowel between the clamps applied at the time of operation and he also advocated a transverse incision. He showed a modified Devine clamp devised by Michael DeBakey, New Orleans, La., which has a lighter superstructure, and he gave the results in 16 cases in which the Devine procedure was used. Dr. Lahey, in closing the discussion of his paper said that he did not do radical operations for benign lesions and added that he did not mean to advocate the Mikulicz operation in all cases as he sees no reason for not employing the one-stage operation in selected cases. He recommended that surgeons start with two-stage and change to one-stage operations as they become more proficient in resections of the large bowel.

Harvey B. Stone, Baltimore, Md., presented a method of surgical treatment for giant rectum and sigmoid. He reported two cases and described the successful treatment employed in one of these cases. In one case it was possible to regulate the bowels without surgical intervention. In the other case, a man who had had an imperforate anus and who had a stenotic opening, local plastic operations were inadequate, so laparotomy was done and the colon was mobilized, after which the patient was turned face down, the intestine around the anus was dissected, and then the bowel brought down and attached to the skin edges. Subsequent introduction of fascial strips to relieve incontinence was only partially successful. He believes that one case was of purely mechanical origin while in the other case there was no mechanical factor. Sympathectomy, he felt, would have done no good in either case. Carrington Williams, Richmond, Va., reported a case similar to Dr. Stone's second case; i.e., a 9-year-old patient who had had an imperforate anus. A colostomy was performed, followed by a fascial sling operation. Dr. Stone, in closing the discussion of his paper, said that he believed a colostomy alone would not have been sufficient in the case he reported.

John de J. Pemberton, Rochester, Minn., considered the anatomic factors of importance in the development of rectal prolapse and asserted that some abnormality of these structures must be present for development of prolapse. Dr. Pemberton reviewed five types of operations for prolapse, choice of which should depend on the condition existing in a specific case. All of the methods described have been intended to be curative, but in all instances there have been some recurrences. He cited reasons for failure of various types of operations, such as the one devised by Moschcowitz. By means of lantern slides he showed a new method which he has employed in six cases.

Ambrose H. Storck, New Orleans, La., presented a résumé of intestinal obstruction due to intraluminal foreign bodies, notably gallstones, fecaliths, enteroliths,

intestinal calculi, food boli, and intestinal parasites. The occult etiology and the sometimes insidious onset of ileus due to foreign bodies have been responsible for a generally high mortality. Indications for conservative or operative therapy in the various types of foreign body obstructions were discussed.

John Gerster, New York, N. Y., in discussing Dr. Storek's paper, considered the toxic substances liberated by dead ascarides harbored by the human as analogous to toxic substances given off by intestinal parasites infesting horses. He cited a case of fecalith obstruction of the descending colon associated with a massively distended cecum which protruded through the operative incision, in which a cecostomy was done.

I. A. Bigger, Richmond, Va., talked about the treatment of suppurative pericarditis and gave the incidence of pericarditis according to autopsy experience as compared with the relatively low incidence of clinical recognition of the condition. He emphasized the importance of frequent examinations of the heart area in septic cases, especially thoracic and subphrenic infections and osteomyelitis. Suspicious physical findings should be confirmed by x-ray. A case treated by repeated aspiration until a total of 900 c.c. of fluid was removed was presented. The diagnosis in this case, which ended fatally, was noninfectious hemorrhagic pericarditis. Attention was called to the danger of puncture of a coronary vessel in doing pericardiocentesis and Dr. Bigger adversely criticized the treatment of suppurative pericarditis by repeated aspirations and sulfanilamide. Early open operation was recommended and the prevention of sacculations of pus by repeatedly passing a gloved finger between the heart and the pericardium was mentioned.

In discussing Dr. Bigger's paper, Alfred Blalock, Nashville, Tenn., emphasized the desirability of early operation and felt that the more extensive operation, including removal of the fourth and fifth costal cartilages and a portion of the sternum, is desirable. He referred to cases of suppurative pericarditis which have been observed in the Vanderbilt Hospital.

Walter D. Wise, Baltimore, Md., especially considering mesenteric lymphadenitis, discussed the apparent or relative incidence of various abdominal lesions, years ago and at present. He added nine personal cases of mesenteric lymphadenitis and cited a high seasonal incidence of this disease entity in August and September. The etiology suggested by various observers, the age and sex incidence, and the clinical picture produced by the acute, subacute, or chronic types of mesenteric lymphadenitis were analyzed.

Mims Gage, New Orleans, La., discussed the incidence of mesenteric lymphadenitis in 65 cases on the Tulane Surgical Service. All these cases occurred in patients in whom chronic appendicitis was suspected, and all were relieved following appendectomy. An enterococcus was found in 90 per cent of the cases.

Frederick A. Collier, Ann Arbor, Mich., presented the results of studies on the reaction of the peritoneum to trauma. He prefaced his remarks with a comment concerning the difficulty of producing satisfactory experimental peritonitis. Contamination at the time of operation on the lower intestine seems to produce some protection for about one month. The study of smears of peritoneal fluid or exudate is a valuable prognostic method.

Fred W. Bailey, St. Louis, Mo., limited the scope of his paper on nonpenetrating intra-abdominal injuries to the factors of shock and hemorrhage, without considering peritonitis. The many severe nonpenetrating wounds resulting from

increasing numbers of automobile accidents require frequently repeated careful examination and study, followed by active therapy when indicated. Some cases are operated upon too soon, others too late. The author indicated the not uncommon difficulty of differentiating between shock and hemorrhage. The simplicity and advantages of the Barbour and Hamilton falling-drop method of determining specific gravity of blood were discussed and Dr. Bailey indicated the value of repeated determinations of this sort as a means of determining the progress of cases of acute abdominal injury. Also, plasma protein and hematocrit determinations may be helpful guides to management. The danger of secondary hemorrhage following spleen injuries was mentioned. The administration of adrenal cortical extract was advocated in certain of the more severe cases.

In discussing this paper, Frank K. Boland, Atlanta, Ga., gave statistics concerning injuries and deaths and cited the high incidence of such injuries caused by automobiles. Dr. Boland spoke about the importance of transfusions and recommended the use of acacia in the meantime. Rettig A. Griswold, Louisville, Ky., observed that at present more rapid transportation results in many critically ill cases coming into hospitals; whereas, formerly such cases died before their transfer was completed. Quick action by a well-organized house staff is important. Alfred Blalock, Nashville, Tenn., discussed the mechanism of shock and reiterated that simply replacing the amount of blood lost will not relieve the symptoms associated with hemorrhage. He explained how shock may be produced by various mechanisms. James M. Mason, Birmingham, Ala., spoke about the difficulty of deciding on the proper management of the severely traumatized individual. Robert S. Hill, Montgomery, Ala., reported four cases which presented no serious abdominal wall injury, but in which serious intra-abdominal injury was present.

T. B. Reeves, Greenville, S. C., reviewed his observations and conclusions concerning the use of appendicoccecostomy in the treatment of peritonitis. The procedure is considered valuable when adynamic ileus has developed. The pathology of peritonitis as well as operative details were presented. He and his associates have done 52 cecostomies in their worst cases of peritonitis, with 6 fatalities.

In discussing the paper, Charles Gordon Heyd, New York, N. Y., emphasized the importance of the appendicitis problem. He advocated the Handley operation; i.e., a jejunocolostomy and a tube colostomy along the ascending colon. Two of 6 patients on whom this operation was performed died. William H. Prioleau, Charleston, S. C., discussed the employment of appendicoccecostomy and cited a mortality of 7 per cent in a group of patients in whom this procedure was used. J. Garland Sherrill, Louisville, Ky., re-emphasized the importance of early diagnosis. Frederic W. Bancroft, New York, N. Y., advised that the drainage tube be passed on into the terminal ileum. Reginald H. Jackson, Madison, Wis., stated that appendicoccecostomy is performed in selected cases in his clinic.

John E. Cannaday, Charleston, W. Va., reporting his observations in regard to the treatment of peptic ulcer, reviewed the etiology, the pathology, and the indications for the various types of management of peptic ulcer. He considered conservative treatment for duodenal ulcer almost always in order.

Joseph D. Collins, Portsmouth, Va., reported a case of trichobezoar with recurrence. From his review of the literature he found 138 cases on record, including his own, with only 3 instances of recurrence. The occurrence of multiple hair balls was also cited. Diagnosis by the history, physical examination, and x-ray findings was considered. Treatment is purely surgical. In the case of recurrent trichobezoar which he reported there were 3 jejunal hairballs, with complicating perforation and intussusception. Ambrose H. Storck, New Orleans, La., discussed Dr. Collins' paper and reviewed statistics and observations resulting

from a study of bezoars and concretions made by Dr. DeBakey and Dr. Ochsner. Frank S. Johns, Richmond, Va., presented 2 bezoar cases which had been previously reported, 1 in the stomach and 1 in the intestine. The first case had no symptoms, but there was a palpable mass. The second case developed intestinal obstruction.

William H. Prioleau, Charleston, S. C., reported the results of thyroidectomy in cases of hyperthyroidism associated with neurocirculatory asthenia. He warned against doing thyroidectomy when neurocirculatory asthenia exists alone.

Edwin P. Lehman, University, Va., gave the results of a study of the duration of preoperative treatment in thyrotoxicosis. His report was based on 401 cases, 111 of which were nontoxic. The importance of determining the optimum point in the preparation of thyrotoxic patient was stressed. Only 3.1 per cent of patients had graded operative treatment. In the University of Virginia Hospital series the incidence of thyrotoxicosis was as great among negroes as among whites. There was a 9 per cent mortality in the negro cases, and the recurrence rate was twice as great in the colored cases. The average duration of preoperative treatment was ten days. Dr. Lehman observed that response to preparation varies greatly. Half of the patients, who on admission seem to be in worst condition, respond much better than certain patients who at the beginning seem less toxic.

In discussing the last two papers, Robert S. Dinsmore, Cleveland, Ohio, expressed the belief that it is difficult to select the type of cases referred to by Dr. Prioleau. He also said that the asthenic symptoms are likely to return after a period of relief, and that tachycardia is likely to persist. If, after an overnight hospital rest, the pulse rate is markedly lowered or comes to normal then he considers that there is no hyperthyroidism. Dr. Dinsmore was surprised at the high incidence of hyperthyroidism among negroes reported by Dr. Lehman. He advised against changing the dose of iodine which a patient has been taking before coming under the surgeon's care because of the danger of upsetting the patient. Frank Lahey, Boston, Mass., gave a résumé of the continued investigations concerning the blood iodine being done in his clinic. They have found that when the blood iodine and the basal metabolic rate come to normal together (70 per cent of cases) the recurrence rate is low. When the return does not run parallel (30 per cent of cases), 20 per cent of the patients have recurrences. A high metabolism with low iodine is associated with a high mortality. With high blood iodine there is a high urine output with a proportionate increased output of iodine, so that at the end of one year the iodine will be low and the patient will be a poor risk. He felt that surgery is of no value in neurocirculatory asthenia. Willard Bartlett, St. Louis, Mo., outlined what he considered the absolute contraindications to thyroidectomy; i.e., (1) cardiac decompensation; (2) psychosis; (3) rapid continuing weight loss; (4) vomiting, diarrhea, and excessive sweating; (5) a rising basal metabolic rate; and (6) a duration of voluntary apnea less than 20 seconds. The latter factor he considers a very important criterion. I. A. Bigger, Richmond, Va., said that he had observed the same high negro mortality rate in hyperthyroidism referred to by Dr. Lehman. He believes it not due to any inherent condition but that factors such as malnutrition, not necessarily subnutrition but perhaps vitamin deficiency, are responsible. James D. Rives, New Orleans, La., explained the unusually high mortality in Maes' report by citing the following: (1) many of the operations were done by occasional operators; (2) mismanagement before admission; (3) high percentage of negroes in the New Orleans Charity Hospital; i.e., 50 per cent; (4) handling of patient in the hospital; i.e., two patients in one bed; (5) high

humidity in New Orleans interfering with loss of body heat. T. C. Davison, Atlanta, Ga., discussed intravenous iodine preparation and also said that he was now doing more radical operations. Dr. Prioleau, in closing the discussion of his paper, said that he expected exception to be taken to what he presented, but he reiterated that he felt that thyroidectomy was justified in his cases. He believes that definite histologic evidence of hyperthyroidism may be lacking in some early cases which are promptly given iodine and then subjected to thyroidectomy.

Charles A. Vance, Lexington, Ky., presented the hazards associated with surgery in the presence of hemophilia. He reviewed the descriptions of hemophilia and drew attention to recent significant experimental work. Four cases were reported; in two cases operation was done and in two cases operation was refused. There was one death in each group. Case 1: Breast carcinoma for which radical breast amputation was done. There was greater than usual bleeding during operation and the skin flaps became elevated after operation. He later obtained a history of hemophilia. Case 2: Patient aged 25 years, who had been known to bleed excessively since 2 years of age. The patient had symptoms of an abdominal catastrophe, due to a gangrenous perforated appendix. Appendectomy was done with careful hemostasis; 500 c.c. of citrated blood was given postoperatively and 500 c.c. of citrated blood was given subsequently. The patient also received fibrinogen, in spite of which the wound filled with blood; 500 c.c. citrated blood was given at a third transfusion, but the patient died. Case 3: Patient aged 19 years, lower right quadrant abdominal symptoms. He has had recognized hemophilia since 8 months of age. Hemorrhages into joints and elsewhere. It was considered that the patient had a better chance for recovery without operation. Treated with theelin, 1 c.c. daily; fibrinogen; and fluids parenterally. Mass could be felt after several days. Passed large dark stools and developed anemia. Blood transfusions given. This patient survived. Case 4: Brother of patient in Case 3, aged 25 years, known to be a bleeder all his life. Acute appendicitis. Theelin, fibrinogen, transfusions, not operated, appendix ruptured. Died after five days. Dr. Vance indicated that the present outlook for control of hemorrhage in hemophilia is much better. He outlined Mills' prophylactic method; i.e., (1) sensitize the patient to a foreign protein and keep the patient always sensitized so that if necessary a skin reaction may be induced; (2) high protein diet as the protein effect on blood is desirable. He did not give other schemes, saying that they would be published in the transactions volume.

Alfred P. Jones, Roanoke, Va., presented a series of unusual spleen cases. Case 1: Splenic anemia, a case reported by Dr. Cushing, the twelfth case of Banti's disease cured by splenectomy. Patient 40 years of age, still living. Case 2: Female, aged 34 years. Mass in upper abdomen. Gaucher's disease. Splenectomy. Case 3: Female, aged 8 years. Agranulocytosis. Splenectomy. Case 4: Child. Anemia, Banti's disease, five transfusions. Splenectomy. Case 5: Female, aged 23 years, Banti's disease. swelling in left upper abdomen. Four transfusions, splenectomy, spleen projected through hernia in diaphragm.

Following the presentation by Dr. Jones, a series of spleen cases were reported. L. Wallace Frank, Louisville, Ky., reported two cases in which splenectomy was done in which there were miliary tubercles of the spleen. Hubert A. Royster, Raleigh, N. C., said that lesions of the spleen are much misunderstood. He recalled three cases of splenic cysts previously reported; i.e., (1) a retention cyst, (2) a hemorrhagic cyst, (3) a tuberculous abscess of the spleen. W. Lowndes Peple, Richmond, Va., reported a case in which the spleen was on a twisted pedicle and was lodged in the pelvis. Reginald H. Jackson, Madison, Wis., cited the absence of the splenic notch as a sign which has been suggested as an evidence of primary neoplasia of the spleen. By moving pictures he showed a hemangio-



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J. Stewart Rodman, Philadelphia, Pa., reported a case of plasma cell mastitis in which a radical mastectomy was done. He stated that in plasma cell mastitis there is pain which is usually absent in carcinoma. The lesion is composed of areas of necrotic tissue and granulation tissue, large numbers of colostrum-like cells containing fatty crystals, and large numbers of plasma cells. This disease occurs in nonlactating women, and may be due to a fat-splitting enzyme. Robert L. Payne, Norfolk, Va., stated that Cheatle was the first to describe plasma cell mastitis. He believed that all the changes in plasma cell mastitis are due to inflammation. In the terminal stage there is a production of large amounts of connective tissue and this stage resembles carcinoma. L. Wallace Frank, Louisville, Ky., reported cases of fat necrosis of the breast and spoke on differential diagnosis. Isidore Cohn, New Orleans, La., reported two cases of carcinoma of the breast occurring in the white male. Mims Gage, New Orleans, La., reported 6 cases of carcinoma of the male breast, 5 cases in negroes and 1 in a white person. He stated that carcinoma of the male breast is much more common in the negro race. He also reported a pure osteoma occurring in the left breast of a 60-year-old white male.

Roy D. McClure, Detroit, Mich., gave a report of 90 operations for femoral hernia. Among the 24,100 admissions to Ford Hospital from 1916 to 1936, there were 4,530 inguinal hernias and 90 femoral hernias, an incidence of 50 inguinal to 1 femoral hernia. There were 60 hernias in the male and 30 in the female; 63 were on the right side and 27 were on the left. Dr. McClure stated that child-bearing was not related to the development of these hernias. He expressed an increasing preference for spinal anesthesia in operations for hernia. The femoral approach (54 cases) was followed by recurrences in 9.7 per cent of cases; the inguinal approach (27 cases) was followed by recurrences in 7.4 per cent of cases; but when the combined approach (9 cases) was employed there were no recurrences. The mortality for the entire series was 4.4 per cent and the average recurrence rate was 7.8 per cent. The operation employed was performed as follows: inguinal approach, potential inguinal sac opened, finger inserted into peritoneal cavity, femoral sac identified, forceps introduced into sac, sac everted and removed, then closure of transversalis fascia and hernioplasty. In the discussion of this paper, Rettig A. Griswold and John W. Price, Louisville, Ky., reported cases, and H. A. Rutledge, Richmond, Va., reported 314 cases with a 10.5 per cent recurrence. With the use of silk, there were 9.1 per cent recurrences; with catgut, 6.2 per cent; with fascia, 27.7 per cent. Robert L. Payne, Norfolk, Va., showed lantern slides demonstrating his method of fascial suture in the repair of femoral hernia, using the inguinal approach.

Walter E. Dandy, Baltimore, Md., reported three cured intracranial carotid aneurysms. He believes that the majority in the young are congenital and that in the aged they are of arteriosclerotic origin. The three cases reported were in the internal carotid canal in the skull. Symptoms consisted of recurrent attacks of severe pain back of the eye and on the side of the head. The onset is sudden and pain is recurrent. There are pupillary changes due to involvement of lymphatics. Treatment employed consisted of the application of a clip on the internal carotid (intracranial) and ligation of the internal carotid in the neck, trapping the aneurysm between these two ligations. The collateral blood supply must be assured before ligation of the internal carotid and is estimated and developed by means of the Matas compressor. Mims Gage, New Orleans, La., in discussing Dr. Dandy's paper, stated that the patient must be able to withstand the compressor for at least one-half hour without cerebral manifestations, before ligating the artery. In the very young adult there is slight chance for

endothelioma of the spleen with absence of the splenic notch. He also reported an infarction of the spleen in a patient with endocarditis. **Robert L. Rhodes**, Augusta, Ga., discussing Dr. Vance's paper, cited a case in which a hemophiliac was just "let alone" and recovered from a severe attack of bleeding. Dr. Vance, in closing, reported a case of splenomegaly of inherited syphilis.

**J. M. Mason**, Birmingham, Ala., spoke about traumatic arteriovenous aneurysms of the great vessels of the neck. Since 1932, 19 arteriovenous aneurysms of various vessels have come under his observation, including 7 cases of the sort presently considered. Transvenous repair of the fistula was possible in 2 cases. He spoke of the cardiac damage associated with such aneurysms, indicated the importance of closing them, and reviewed the various methods which have been employed.

**Isidore Cohn**, New Orleans, La., presented a paper on arteriovenous aneurysm of the femoral artery and reported the case of a patient who was able to return to work. The large heart diminished in size following operation and there was also postoperative electrocardiographic evidence of improvement. Multiple ligations and extirpation were performed because of inability to find a line of cleavage between the vein and the artery and because there were calcareous deposits in the wall of the artery.

In the discussion of the papers presented by Dr. Mason and Dr. Cohn, **Mont Reid**, Cincinnati, Ohio, referred to multiple fistulas which may be produced by gunshot injuries. **Mims Gage**, New Orleans, La., spoke of the effect of arteriovenous fistulas on the heart and cited experimental work done with Dr. George Herrmann; one dog lived seven years with an arteriovenous fistula. He reiterated the observation that the pericardium does not prevent cardiac dilatation. He alluded to a case of internal carotid fistula treated by ligation and excision of the aneurysm and also discussed the value of sympathetic nerve interruption or injection procedures in conjunction with the surgical treatment of aneurysms. **John W. Price, Jr.**, Louisville, Ky., discussed a method of performing vascular anastomosis which he used in experimental work. In a lesion distal to the profunda, involving the femoral artery and vein, he operated after three weeks and did multiple ligations and excisions, since no other type of operation seemed feasible. **Joseph E. J. King**, New York, N. Y., reported four femoral arteriovenous fistulas, all below the origin of the profunda. Quadruple ligation was done in all cases and all recovered with good results. In no instance had more than three months elapsed since the injury. **Edgar L. Gilcreest**, San Francisco, Calif., gave a progress report on a subclavian aneurysm case previously reported and now doing well. He emphasized the importance of relieving edema by elevating the arm. **Reginald H. Jackson**, Madison, Wis., reported two cases of femoral aneurysms which were approached distal to a tourniquet applied above Wyeth pins.

**John S. Horsley, Jr.**, Richmond, Va., presented a paper entitled *Benign and Malignant Lesions of the Male Breast*. He stated that the male breast is not a rudimentary organ, but contains all of the elements of the female breast, and that from a microscopic standpoint the tumors developing in the male breast are indistinguishable from lesions of similar character occurring in the female breast. Forty-one breast cases occurring in males and 944 cases in females were reported to show the sex incidence. Chronic cystic mastitis: males, 23; females, 332; malignant tumors: males, 4; females, 359; hypertrophy of breast: males, 2; females, 3. Of the malignancies of the male breast the youngest was 13 years old and the oldest was 73 years old. There were four malignancies of the male breast. He stated that the prognosis in the male is better than in the female because the lesion is more easily recognized and therefore can be diagnosed earlier.

is important. Routine use of a bulb in investigating the upper urinary tract is important. X-ray is of little help in diagnosing stricture of the ureter. Routine dilatation of the ureter is the best treatment of this condition.

W. F. Shallenberger, Atlanta, Ga., spoke about conservative pelvic surgery. Conservative measures are often more trouble and more difficult, technically, than radical measures. A study of each case is necessary and development of technique is important. Conservation of part or all of the ovary in cystic diseases is important. The use of radium and myomectomy in the treatment of fibroids was stressed.

John T. Moore, Houston, Tex., presented a paper on *An Improved Method of Vaginal Hysterectomy for Prolapse of the Uterus*. This operation was originally described by Dr. L. L. Shropshire, of San Antonio, Tex. Rubber-covered clamps are placed on each side of the uterus; the uterus is sectioned on each side in its wall but outside of its lumen; the uterine slabs are then approximated by mattress sutures. The uterus is replaced in the abdomen and an anterior colporrhaphy done. If this does not give adequate support, a Watkins interposition operation is done on the remaining uterine segment. The operation preserves the vascular and nerve supply of the uterus. He thinks that the procedure is better than the Mayo technique because the possibility of herniation is less, but he does not advocate it routinely in prolapse; he still does some facial supports. Emil Novak, Baltimore, Md., discussed this paper, saying that in this country the abdominal route is the most popular, while vaginal hysterectomy is popular on the Continent. He has never done Dr. Moore's operation, but he has done a defundectomy in the course of doing a Watkins operation. He felt that no harm comes from disturbing the blood and nerve supply in doing a vaginal hysterectomy. He thought that Dr. Moore's operation was as good as the orthodox vaginal hysterectomy. Dr. Moore, in closing, said that he thinks the slabs of uterine tissue have a constitutional endocrine value.

Quitman U. Newell, St. Louis, Mo., spoke about injury to the ureters during pelvic operations. The author stated that in 3,144 hysterectomies performed at Barnes Hospital since 1915, the ureter was injured in 15 cases. The early recognition of the injury is important. Transplantation of the ureter into the bladder is not satisfactory. Dr. Newell favors an end-to-end anastomosis.

cerebral complications due to the rapid development of the collateral circulation. Dr. Gage suggested that the stellate ganglion be injected or even removed surgically, and if necessary that the stellate be attacked bilaterally to augment the collateral circulation by releasing vasomotor control of the cerebral vessels. Ernest Sachs, St. Louis, Mo., reported three cases of intracranial aneurysm. One patient died following the application of the Matas band to the internal carotid. The patient tolerated compression for ten minutes, but when the band was applied the patient developed hemiplegia. The band was removed but the patient died thirty-six hours later.

Joseph E. J. King, New York, N. Y., presented a paper entitled *Epidermoid (Cholesteatoma) Tumors of the Central Nervous System*. He considered only those intracranial epidermoids arising from the diploe. They constitute 0.6 per cent of brain tumors. The x-ray reveals a tumor with scalloped edges. The cholesteatoma has three layers: (1) fibrous, (2) epithelial, and (3) desquamated epithelium and debris. He reported 6 personal cases, 5 intracranial and 1 spinal. All were operated upon and proved histologically. He described the gross pathology and the technique of removal. Gilbert Horrax, Boston, Mass., discussed this paper and in speaking about dermoids said that they are frequently infected, thus complicating the operative procedure.

Edgar F. Fincher, Atlanta, Ga., considered the neurosurgical aspects of low back pain and sciatica. The known causes of low back pain are increasing and the diagnosis is becoming more complicated, the latest addition being rupture of the nucleus pulposus. He reported one case due to melanoma of the sub-arcuoid and vertebra. The inguinal glands also contained a melanotic growth. Another case reported was due to a bullet lying on the sciatic nerve, with chronic osteomyelitis of the femur. A detailed history is most important in the differential diagnosis. He reported 50 cases of herniated nucleus pulposus; 70 per cent of these cases gave a history of injury; 11 cases did work which contributed to back trauma. The 50 cases presented all of the usual neurologic signs and symptoms. There was a history of pain in the back radiating to one or both thighs. Tenderness between spinous process at site of herniation occurred in all cases. Dr. Fincher used lipiodol intraspinaly and epidural injection of air to demonstrate the site of the lesion. He suggested that this latter method should be used more frequently instead of lipiodol. In operating, he performed unilateral laminectomy and allowed the patient up in a few days. Results in all cases were excellent.

Deryl Hart, Durham, N. C., spoke about the reduction of postoperative temperature reactions obtained by sterilizing the air with bactericidal radiant energy, especially from the standpoint of the effect of summer heat and perspiration. Wound healing was more perfect, and infection was reduced to a minimum. Length of stay in the hospital was shorter and postoperative temperature reactions were reduced. Reginald H. Jackson, Madison, Wis., stated that all surgical wounds are contaminated and should be treated as such. He showed a moving picture demonstrating his method of treating surgical wounds. Waltman Walters, Rochester, Minn., said that the Society should accept the method of Dr. Hart for consideration. He suggested to Dr. Hart the study of the effect of the light on the blood pressure, fatigue, skin, blood, and glands of internal secretion of the operating surgeon. He further suggested that the Association have a symposium on the control of infection in operating rooms.

Guy L. Hunner, Baltimore, Md., discussed the treatment of congenital cystic kidney by means of ureteral drainage. The surgical and medical treatment of this condition is unsatisfactory. Stricture of the ureter is present in most cases of congenital cystic disease of the kidney. The early diagnosis of this condition

its favor. Even though intended primarily for the undergraduate student and general practitioner, the absence of references in this text is a serious omission. Osler employed commonly the scheme used frequently in physiologic literature of inserting the year after a quotation from an author, such that the earnest student desiring a more intimate acquaintance with the subject under discussion could find it readily in available indices, a practice which the new author unfortunately has not deemed it worth while to continue.

It is to be hoped that if the present editor of Osler's *Principles and Practice of Medicine* undertakes a new revision that he will avail himself of the assistance of others who will divide the burden and enhance the value of this important and substantial text.

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**A Textbook of Gynecology.** By Arthur Hale Curtis, M.D., Professor and Chairman of the Department of Obstetrics and Gynecology, Northwestern University Medical School; Chief of the Gynecological Service, Passavant Memorial Hospital, Chicago, Ill. Ed. 3. Cloth. Pp. 603, with 318 illustrations. Philadelphia and London, 1938, W. B. Saunders Company. \$7.

The first edition of this book was published in 1931 and contained 362 pages and 322 figures. The present edition contains over 600 pages and 318 figures, many colored. In the present edition the author has given up the plan of his first edition in which he reported only his own views. He now presents a composite view but wisely emphasizes his own beliefs. Several new chapters have been introduced. The chapter on anatomy presents this subject from the viewpoint of the gynecologist rather than the anatomist and is for that reason of great value to both student and gynecologist. The subject of gynecology has been covered in its entirety. Surgical procedures and medical treatment are presented when indicated. The only criticism which the reviewer could possibly make would be the need of the insertion of a few more illustrations in the section on technique of total hysterectomy. The book is highly recommended.

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**Sulfanilamide Therapy of Bacterial Infections: With Special Reference to Diseases Caused by Hemolytic Streptococci, Pneumococci, Meningococci, and Gonococci.** By Ralph R. Mellon, Paul Gross, and Frank B. Cooper. Pp. 398. Springfield, Ill., 1938. Charles C. Thomas, Publisher. \$4.

Sulfanilamide and its related compounds were introduced into this country the latter part of 1936. Employed originally for the treatment of hemolytic streptococci sepsis, they have been found effective for a variety of bacterial infections. Within a short period of time, a voluminous literature concerning this new chemotherapy has confronted the medical profession. The present volume is, in part, a review of this literature, and a presentation of investigative work that has been carried on at the Institute of Pathology of the Western Pennsylvania Hospital.

The work is divided into four sections. Section I includes a good summary of the chemistry and pharmacology of sulfanilamide and similar compounds. Succeeding chapters review the experimental results and the clinical applications of these drugs, with particular reference to the hemolytic streptococcus, pneumococcus, meningococcus, and gonococcus. Section II is a review of the authors' experiments and clinical results with sulfanilamide in streptococci and pneumococci infections. Their work with the streptococcus confirms the work of many others. Evidence is presented to show that sulfanilamide will protect animals infected with pneumococci.

## Book Reviews

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**Fractures of the Jaw.** By Robert H. Ivy, M.D., D.D.S., F.A.C.S., Professor of Maxillo-Facial Surgery, Graduate School of Medicine, and of Clinical Maxillo-Facial Surgery, School of Dentistry, University of Pennsylvania, and Lawrence Curtis, A.B., M.D., D.D.S., Assistant Professor of Maxillo-Facial Surgery, Graduate School of Medicine, and School of Dentistry, University of Pennsylvania. Ed. 2. Pp. 192, with 199 illustrations. Philadelphia, 1938, Lea and Febiger, \$4.50.

This second edition should continue to receive wide acceptance as a standard reference for fractures of the jaws. Anatomic descriptions and illustrations are clear.

Descriptions of all types of fractures are given, beginning with the simpler and more frequent ones. Treatment is given clearly and with fairness to all acceptable types of procedures, but one is glad to find definite views of the authors throughout. Although no claim is made for having combed the literature, this undoubtedly has been done. One who has tried to arrive at a standard set of conclusions by covering the endless amount of ideas in the literature will accept this work with great relief.

The general surgeon, oral surgeon, dentist, and roentgenologist all will find usable methods advocated for their respective fields in the care of fractured jaws.

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**The Principles and Practice of Medicine—Designed for the Use of Practitioners and Students of Medicine.** Originally written by the late Sir William Osler. Revised by Henry A. Christian, Harvard University, Boston, Mass. Ed. 13. Pp. 1424, with 1 illustration. New York, N. Y., 1938, D. Appleton-Century Company. \$9.

Osler's textbook of medicine appears now in the thirteenth edition under the editorship of Henry A. Christian, Physician to the Peter Bent Brigham Hospital in Boston. It is interesting to turn the pages of this and former editions and to note changes in subject matter which have come with the years. It is startling to note how much of the skeletal structure worked out by Osler remains still. There are diseases where the growth of knowledge is reflected in more specific treatment and new points of view. It is somewhat discouraging to note the number, however, of which this cannot be said.

Present-day American teachers of medicine and surgery were probably all reared on Osler's text of medicine, and it is very reassuring to see an eminently practical and useful book sustain its popularity well into a new generation.

In his preface, the new editor states: "In preparing this revision, wisely or unwisely, I have had the assistance or criticism of no one." Much as the present reviewer is devoted to Osler's *Principles and Practice of Medicine*, he is definitely of the opinion that the new editor would have gained much for this thirteenth edition by availing himself of the help of acceptable authorities in special fields. Medicine has outgrown any one man's knowledge. Despite the disadvantages of varying styles and different points of view apparent in the text of multiple authorship, the advantages of more authoritative and exact information weigh heavily in

# SURGERY

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## Original Communications

### COMPLETE TEARS OF THE PERINEUM

PREPARATION, OPERATIVE TECHNIQUE, AND TREATMENT AFTER OPERATION

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*(From the Department of Gynecology, School of Medicine, Tulane University)*

A SURPRISINGLY large number of failures continue to occur in the management of complete or so-called third degree tears involving the rectovaginal septum and the sphincter ani muscles. These failures are due in some part to the technique used and again to the neglect of apparent trifles in the treatment after operation for repair.

Complete laceration of the female perineum is a subject as old as the beginnings of gynecology and one that frequently has been described and discussed. The earliest account that we find of an operation for a completely ruptured perineum is by Trotula, renowned woman physician and teacher of the School of Salerno in the eleventh century. The uterus, if prolapsed, must, she directed, be softened by hot wine compresses and replaced and the tear itself at once sutured. A tampon soaked in hot wine and butter was to be placed in the vagina, to retain the uterus, while deep stitches were to be taken at the anus, and in three or four other places, with silk thread, and the whole was to be well dusted with powder. Then a linen cloth soaked in tar water was to be tightly bandaged against the wound, and the patient's feet held "higher than the head." She was to be kept in this position for eight or nine days without bathing. She was not to be allowed to vomit, and her diet was to be very simple. Knowing, of course, nothing of sepsis, Trotula yet directed that pads were to be placed against the anus, or in the rectum, to prevent any contact with feces. But Trotula sensibly concludes: "Although the perineum will be stronger than before it was torn, it would have been better to avoid such injury by greater care at the birth of the baby."

During the eight hundred years since Trotula's book on gynecology was written, interest in complete perineal injuries has had many re-

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A small number of human cases with Type III pneumococcic pneumonia were treated with sulfanilamide and only suggestive evidence is presented that the drug was effective. It is stated that "vitamine—hormone reinforcement" of patients severely ill with pneumonia should accompany sulfanilamide therapy, and inadequate data are presented to verify this opinion. Section III is devoted to a discussion of the mode of action of sulfonamide compounds. Precise information on this point is still forthcoming. Further controversial material is introduced when it is implied with insufficient evidence that sulfanilamide may play a role in the dissociation of bacteria. As an example, hemolytic streptococci may dissociate into diphtheroids. Section IV concludes with a general discussion of chemotherapy and the factors determining therapeutic efficiency.

The authors cite 305 references. They have reviewed the literature well, but have presented the results of some of their own investigative efforts without adequate data to support their conclusions.

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**Applied Anatomy, Functional and Topographical.** By Robert H. Miller, M.D., Associate Professor of Anatomy in the University of Tennessee, College of Medicine, Memphis, Tenn.; Formerly Associate Professor of Surgery in Charge of Operative Surgery; Formerly Attending Surgeon to the Memphis General Hospital, Memphis, Tenn. Pp. 484, with 55 engravings and 16 color plates. Philadelphia, 1938, Lea and Febiger. \$6.50.

"This volume attempts to correlate the facts gained by observation in the laboratory and apply them to the dynamics and function of the living body." In order to review fairly a book, it is necessary to know to whom the book is addressed, for what purpose it was written. It is difficult to answer these questions about this volume. If the medical student in his clinical work should wish to refer to this *Applied Anatomy* after he has heard his surgical instructor discuss the relations of the thyroid gland, he would find no mention of the recurrent laryngeal nerve and he would see in the illustration to which he is referred only a posterior view of the gland, labeled "parathyroid glands." If he wishes to know why a rigid catheter is depressed after it has been passed for a certain distance in order to pass it into the bladder, he will look in vain for an anatomic explanation.

The sections on the skin and the organs of the special senses are entertainingly written and seem to the reviewer the best portion of the book. The illustrations are few and for the most part do not come up to the standard we expect in a modern publication.

cause of obstetric injury sometimes as recent as two or three years, and more often dating back as far as ten, fifteen, and even twenty-nine years.

Incontinence of gaseous and fecal contents may or may not be an immediate result of perineal laceration. Some patients in this group reported a gradual loss of control extending over several years and a great number had endured complete absence of sphincter control over even a longer period of time. Diarrhea may develop after a long period as a result of complete perineal tears and frequently this symptom is the first complaint of the patient. It is always a matter of astonishment that so many women endure such a depressing and unsupportable condition to seek relief only when the acute stage of pain and discomfort is reached.

Uniform preparation and aftertreatment and, with a few exceptions, the same operative treatment were carried out in all the cases in the present series of sixty-three patients operated upon during the last seven years. The final results of the operations performed by Miller and by myself are given in Table II.

TABLE II\*

	CHARITY HOSPITAL	TOURO INFIRMARY	TOTAL	PERCENTAGE
Perfect control	25	24	49	86%
Partial control	3	4	7	12%
Failure	0	2	2	2%
No information upon final result	2	3	5	
	30	33	63	

\*Failure in one of the cases was due to the patient's having been given an enema the day following operation contrary to our direct instructions. This points out the necessity for the house staff and nursing service to follow definite orders as to the postoperative care of these patients.

*Preparation Before Operation.*—The three main objects of any measure taken in the preoperative preparation of patients with third degree lacerations of the perineum are to insure evacuation of the bowels, to facilitate maintenance of constipation for several days after operation, and, as nearly as possible, to guarantee a sterile operative field.

Hospitalization as a rule is not feasible until the day prior to operation. After admission to the hospital, liquids only are allowed. Treatment should begin twenty-four hours before operation when a dose of castor oil is given and only liquids by mouth are permitted until the time of operation. As an additional routine measure, an olive-oil and glycerin enema and a lysol douche are given in the early morning of the operative day. When the patient is under anesthesia in the operating room, the parts are thoroughly cleansed with soap and water and the field is irrigated.

I do not favor spinal anesthesia because it produces too much relaxation of the tissues. After reuniting the severed muscles under spinal anesthesia, the muscle tone is lost and the surgeon is unable to determine

vivals. Techniques and treatments of various sorts have been introduced with the usual tilts between the reactionaries and the radicals. However, in recent years there has been a marked dearth of literature on repair and the end results of complete tears of the perineum. This may be due to the fact that too much is taken for granted or it may be that confusion still exists. But the fact is that failures do continue to occur, many of which could be avoided.

The operation for repair is one that requires the most meticulous and delicate surgical procedure and the most cautious and painstaking post-operative treatment, an operation depending upon these two factors and to some extent upon the degree of preoperative preparation. In the year 1873, when Thomas Addis Emmet apologized for harping on so old a subject as this, he started a new era for the technique for repair of the pelvic floor. At that time he remarked that for years his attention had been occupied with trying to unravel the cause of failure in uniting the torn sphincter and muscles and to devise some means of obviating this failure, adding that "to appreciate so simple an explanation has cost me more thought than any other point in the whole field of the branch of surgery to which I have devoted myself."

The late C. Jeff Miller remarked shortly before his death in 1936 that he did not know of any condition in which more failures occurred than this. The sixty-three cases in the present series are from his services at Charity Hospital and Touro Infirmary, in New Orleans, during the years 1931 to 1935 inclusive and from my personal cases from 1931 to 1938.

TABLE I

	CHARITY HOSPITAL	TOURO INFIRMARY	TOTAL
1931	3	3	6
1932	4	7	11
1933	7	2	9
1934	13	5	18
1935	3	7	10
1936	3	2	5
1937	2	2	4
	35	28	63

There is a prevailing belief that improved obstetrics has greatly lessened the incidence of complete perineal lacerations. This point is debatable. The loss of sphincter and muscle control is not always caused by faulty obstetrics. In two cases in this series loss of anal sphincter control resulted from accidental removal of segments of these muscles during previous hemorrhoidectomies. One case in this series, a girl 10 years of age, was the result of rape. The history, however, of the majority of patients with complete tears of the perineum reveals the

preceding operation. In no case were there more than two or three days of hospitalization previous to operation.

*Technique of Operation.*—Injury is always a variable factor. The choice of operative closure must depend upon the extent of damage to the structures involved. The final test of any procedure is its adaptability to the individual case and whether or not its use will effect restoration of sphincter control.

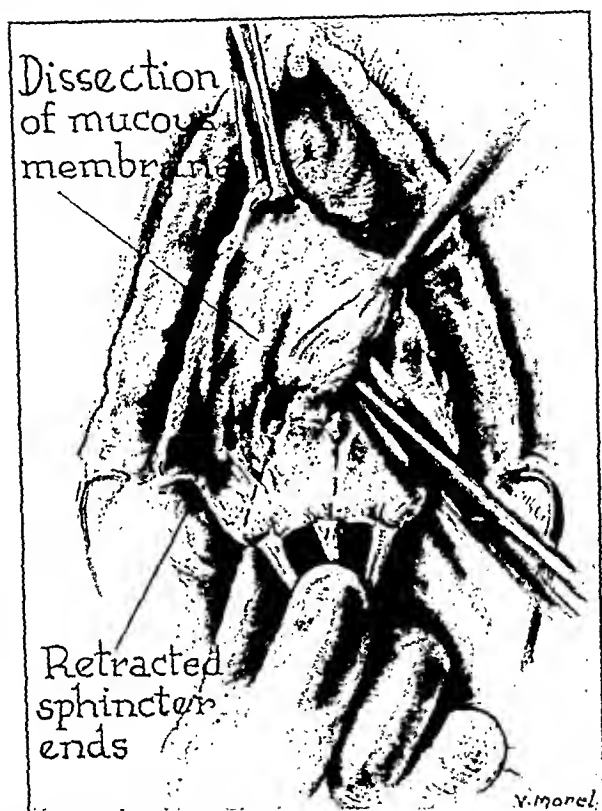


Fig. 2.—Mucous membrane is carefully dissected with scissors. Index finger is inserted into the rectum to facilitate the freeing of the mucous membrane from the scar tissue, also as a protection for the anterior wall of the rectum. A Gelpi self-retaining retractor is used throughout the operation.

When lacerations have existed for many years and considerable atrophic change has taken place in the sphincter ani muscles, fascia lata grafts, as recommended by Harvey Stone, or Sistrunk's method of uniting the ends of the torn sphincter ani muscles with the levator ani muscles will give almost perfect results. Ristine and Noble's operation is usually successful when the injury lies above the anal orifice. As in the Emmet or the Hegar perineorrhaphy, the anterior portion of the rectum is widely separated from the vaginal structures and the freed bowel is drawn down until the tear lies outside the sphincter ring.

whether or not the severed ends have been approximated. Therefore, some form of inhalation anesthesia is advised.

Should the patient be hospitalized earlier than the day before operation, preparatory measures are to start upon admission. Miller advised a series of high irrigations of the bowel and cleansing donches several days prior to operation. The patient should remain in bed during this period and a nonresidue diet should be maintained. The more thoroughly the preoperative treatment is directed toward evacuation of the

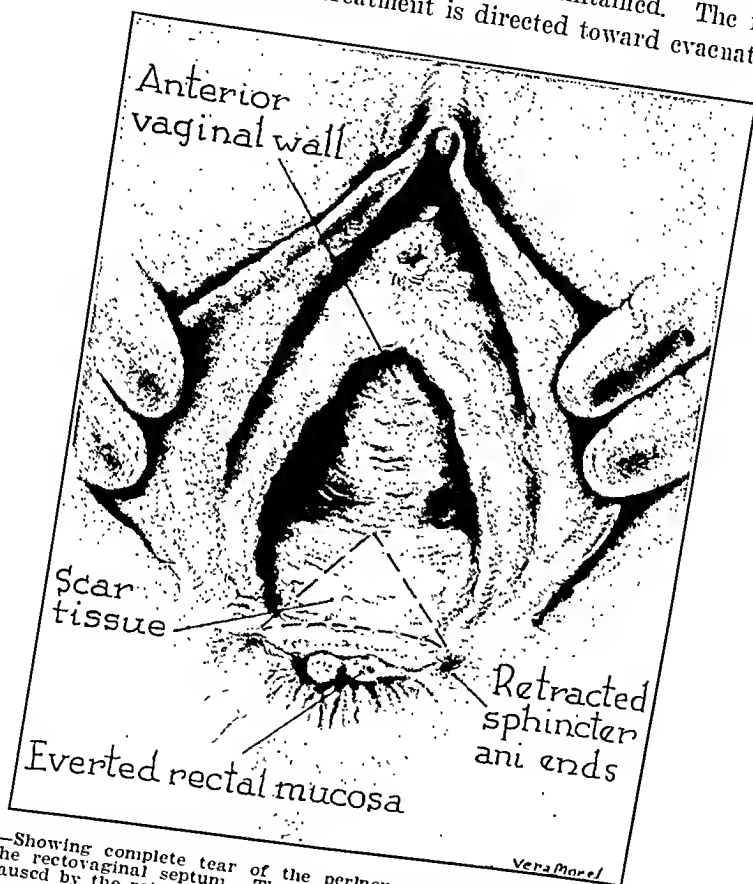


Fig. 1.—Showing complete tear of the perineum with excessive amount of scar tissue in the rectovaginal septum. The rectus mucosa is everted. The pits or depressions caused by the retraction of the sphincter ani muscles may be observed.

bowels and producing constipation, so much easier will it be to prevent defecation after operation, until the desired number of days, and to avoid consequent contamination of the field and any strain upon the sutures. When care is taken to provide a mechanically sterile field, there is less danger of infection from sloughing and formation of stitch abscesses that may become rectovaginal fistulas.

In all cases in the present series this preoperative routine was followed and with but a few exceptions the patients were hospitalized on the day

preceding operation. In no case were there more than two or three days of hospitalization previous to operation.

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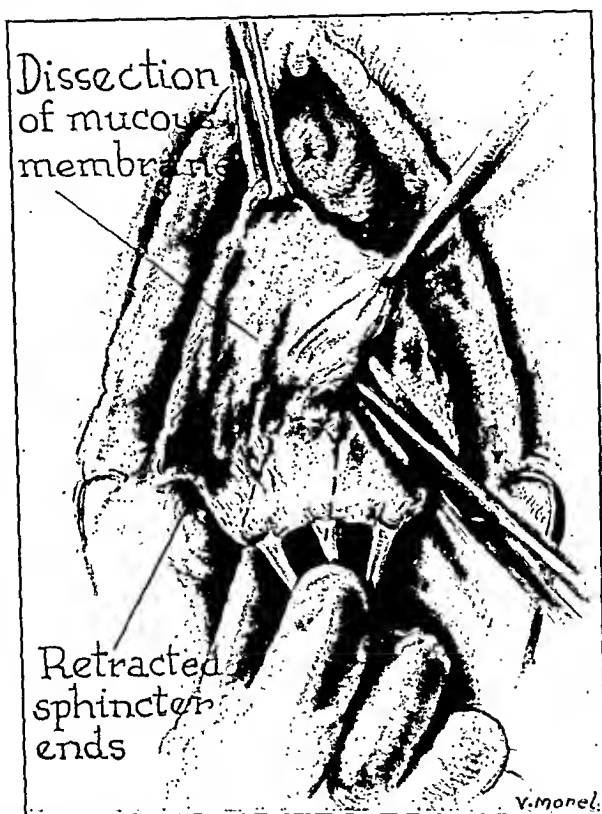


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Sutures may be inserted in this position, after which the sphincter ends are united and the usual perineorrhaphy is followed. The important advantage in this technique is that a line of suture does not remain in the rectovaginal septum. The operation, however, is applicable only to tears that do not extend high into the rectal wall. It is quite surprising how easily the bowel may be slid downward after free dissection and this technique is preferred to the Warren or the Farrar operation which necessitates the creation of a flap, or apron, from the vagina. This apron frequently will slough off because of circulation disturbances and an inexperienced operator by chance may "buttonhole" the flap in his dissection when such a tedious method is followed.

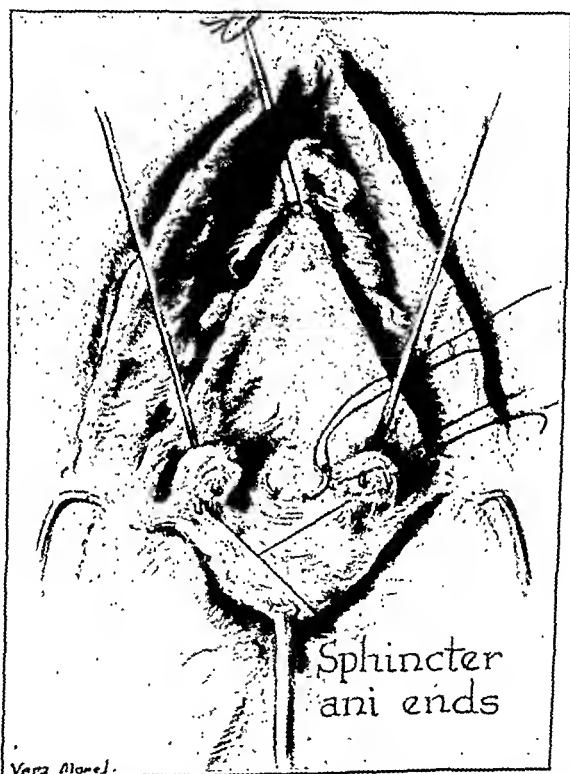


Fig. 3.—After careful dissection of the mucous membrane, allowing the rectal wall to be pulled down, the torn ends of the sphincter ani muscles are located by probing with hooks. A chronic No. 1 suture through the torn sphincter ani muscle ends is passed through the muscularis layer only of the rectal wall. This prevents retraction of the rectal wall above the reunited sphincter.

When the injury extends high within the rectum, or when there is an excessive amount of scar tissue to prevent mobilization, as is necessary in the Ristine-Noble procedure, the rectum and the vagina are separated as in the first steps of a perinorrhaphy. The tear in the rectal wall then is closed by a layer of fine linen sutures within the bowel and inverted (as is done with a Lembert intestinal suture) by a second layer of

chromic catgut sutures placed and tied on the vaginal side. After the sphincter ends are dissected and reunited, the perineal tear is repaired. This operation is the choice when the tear is recent and it is almost invariably the ideal technique for the majority of old lacerations.

The following precautions should be observed no matter what technique is followed: (1) free dissection and excision of all scar tissue; (2) sutures inserted to allow for swelling and to guarantee freedom from tension along the suture line. Quite often, after the sutures have been tied, it appears as though so much tension might interfere with the blood supply. The danger is usually from too much blood supply rather than from not enough so that after the sutures are tied we often make small, so-called "pie-crust" incisions, through the superficial skin layers of the perineum to permit the escape of ooze. This treatment proves of great value in the presence of edema or of tension.

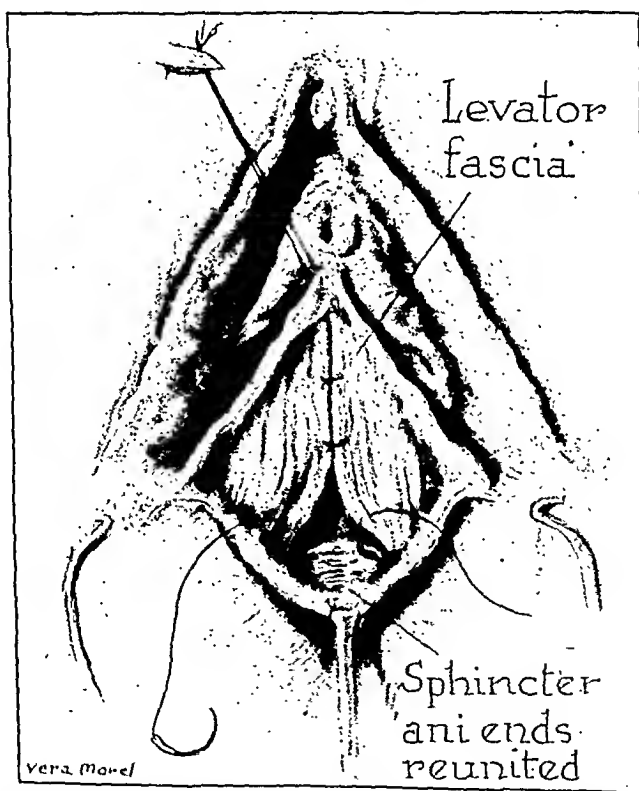


Fig. 4.—The sphincter ani ends have been reunited and the levator fascia and muscle are now closed with interrupted chromic No. 1 sutures. The last suture is passed through the reunited sphincter ani muscle.

Dead spaces are to be carefully avoided. After insertion of the final catgut sutures, four or more silkworm-gut sutures are placed from the perineal side to act as a splint should the catgut sutures break down from too much tension. The lowest suture passes through the ends of



the restored sphincter. The ends of these silkworm-gut sutures are gathered together at the top of the perineal wound and tied into one bunch by the topmost suture. In this way postoperative cleansing of the wound is simplified.

Chromic No. 1 catgut was used throughout this series of cases for uniting the ends of the sphincter ani and the levator ani muscles. Silkworm sutures were used to supplement these. When necessary to suture a tear in the rectum, fine linen was used with interrupted sutures and the ends tied within the rectum. No special dressing is required. The application of a simple perineal pad offers ample protection of the wound.

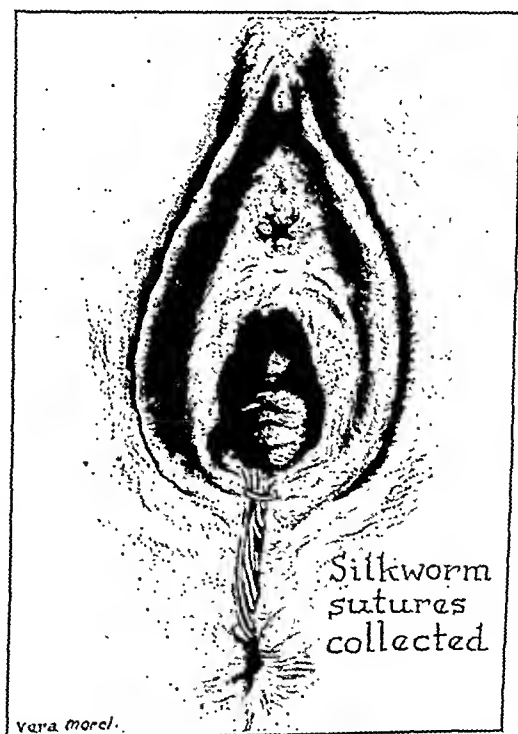


Fig. 5.—Final step shows the silkworm-gut sutures that have closed the perineal incision and extended to the forehette where they are gathered together and brought forward with one catgut suture to hold them together. This facilitates cleansing of the perineum postoperatively and prevents irritation during healing.

*Postoperative Treatment.*—The two principal aims are (1) to insure that there will be no bowel movement for at least seven days after operation, (2) to keep the operative field as mechanically clean as possible. Royston and other writers believe the optimum time for the first defecation to be between eleven and fifteen days after operation. In my opinion one week is usually adequate to obtain satisfactory results.

Beginning the first day after operation and continuing for six days, opium pills (1 gr. three times a day) are administered. In some cases

paregoric is substituted. The patient is kept on a nonresidue diet for as long as the opium is given; i.e., six days to one week and longer if it is found advisable. The nonresidue diet consists principally of water, tea, and coffee, and it does not include fruit juices which are prone to produce gas. In conjunction with the opium, this diet seems to appease the patient's appetite and causes no discomfort.

To maintain cleanliness, the patient is turned on her left side three or four times a day and the perineum is cleaned externally with a solution of potassium permanganate (1:10,000) or bichloride of mercury (1:10,000) or with a weak lysol solution, applied with cotton pledgets. The area is then dried and dusted with aristol powder or boric acid powder. Compresses of boric acid may be applied to the perineum to guard against infection. Royston thought it inadvisable to use pitcher or cleansing douches of any kind and that the wound should be left untouched. He stated that Plass proved twelve or thirteen years ago that untreated repairs heal best. Catheterization is often necessary, but it is better to have the patient void normally as fresh urine is seldom contaminating. Douches and enemas are absolutely not indicated until after the healing is completed nor should a rectal tube be used.

When it is desired to open the bowels on the seventh or eighth day, or later if circumstances so indicate, the patient should be given a cathartic, sometimes preceded by mineral oil. Castor oil is preferable to a saline purgative because the latter produces a liquid stool and does not soften the hard masses which are apt to form in the bowel after it has been kept constipated for seven days, and which are apt to put too much strain on the newly united ends of the sphincter muscles. In order to facilitate a defecation by softening the hard masses, we have found it advisable to instill two or three ounces of warm olive oil into the rectum with a small catheter when the patient feels the impulse to move the bowels. There is less tension if defecation occurs with the patient turned on her side.

The patient is placed on a soft diet when the bowels have acted well and a daily laxative or mineral oil is given, or when both are given so that the consistency is kept soft. If the area of repair is very extensive, the bowel movements should occur in the recumbent position for sixteen or eighteen days, and it is an additional measure of safety to continue the use of the bedpan even beyond this period. The patient should remain in bed for at least two weeks postoperatively.

A rise in temperature must be considered a danger signal of possible infection until it is proved to be otherwise. Compresses of hot boric acid or bichloride of mercury solution should be constantly kept applied to the perineum if infection is suspected. Should the catgut sutures break down, the silkworm-gut sutures, which are deeply placed, prevent separation of the suture line, and if infection can be controlled a successful outcome may still be expected.

Watchful care for ten or twelve days following operation is essential to the successful outcome of the operation. The importance of securing experienced nursing care cannot be overemphasized.

#### SUMMARY AND CONCLUSION

Review of 63 cases of complete tear of the perineum showed perfect control of anal sphincter in 49 cases, or 86 per cent; partial control in 7 cases and only 2 failures.

Success in obtaining perfect results is dependent upon preparation, upon the choice of operative procedure, and, to a very great extent, upon treatment after operation.

In order to provide complete restoration of the lost sphincter control, the operative procedure chosen should be the one best adapted to the extent of damage of the structures.

Treatment following operation should assure that there will be no bowel movement for at least seven days after operation, or until healing is effected; and that the perineal region be kept as nearly sterile as possible, at the same time avoiding the traumatizing effects of enemas, douches, and rectal tubes.

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# AGGLUTININS IN THE SERUM AND BILE OF DOGS FOLLOWING CHOLECYSTITIS PRODUCED BY INJECTIONS OF TYPHOID BACILLI

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THERE is no specific etiologic factor known in cholelithiasis. Both cholecystitis and gallstones are known to be associated with infection. Typhoid fever, for example, has often been followed by cholelithiasis in the presence of a typhoid cholecystitis. In this paper the problem of infection and its relation to stone formation have been studied with respect to the immune bodies found in bile in the course of an experimentally induced typhoid cholecystitis.

Cushing,<sup>1</sup> who studied this subject in 1898, could not demonstrate antibody to be present in bile. However, in 1930, Freund and Henderson<sup>2</sup> showed that if immune serum was injected intravenously in rabbits the antibody could be found in bile. Although the intracholecystic agglutination of bacteria by specific antibody in bile might be a factor in stone formation, there are no reports in the literature indicating the correlation between the presence of infection in the gall bladder or elsewhere, the presence of antibody in bile, and the formation of gallstones. In the experiments reported in this paper the agglutinin titers of serum, gall-bladder bile, and hepatic bile were determined following the introduction of living typhoid bacilli into the gall-bladder wall. In a later paper we will report the data obtained in a clinical study of agglutinins in the gall-bladder bile of patients with biliary tract disease.

## METHOD

Healthy, mongrel, female dogs were anesthetized with ether or sodium amytal. All operations were done under aseptic conditions. An upper right paramedian incision exposed the gall bladder and biliary ducts. The fundus of the gall bladder was isolated, with abdominal pads, and a portion of the gall-bladder bile was aspirated through a fine hypodermic needle (No. 22 gauge).

The subserous layer of the gall bladder was then infiltrated with 2 c.c. of an active twenty-four-hour culture of typhoid bacilli. This injection was done at a distance of 3 to 4 cm. from the original site of aspiration. Fine silk was used to ligate each puncture wound, and the abdomen was closed by tier suture.

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At the close of the observation period, which varied from six to twenty-eight days, another aseptic laparotomy was performed. The abdomen was opened through a right lateral rectus incision to avoid the previous scar. The gall bladder, biliary ducts, and duodenum were examined and the gall bladder was isolated by packing. The contents of the gall bladder were aspirated and the site of puncture was clamped. Cholecystectomy was then performed, following which the common duct was doubly intubated after the method of Rons and McMaster.<sup>3</sup> The abdomen was then closed by tier suture after providing stab wounds for the tubes leading from the proximal and distal portions of the common duct. Hepatic bile was collected under aseptic precautions during twenty-four-hour intervals. After several days the tubes were connected and the bile was allowed to flow into the small intestine.

Venous blood was obtained from each animal at the time of the experimental infection, at intervals during the experiment, and at its conclusion. The serum was used for estimation of circulating antibody.

A portion of each specimen of serum and bile was inoculated into beef infusion (pH 7.4) and the cultures and the centrifuged specimens of bile were examined by Gram's stain.

The agglutination tests were performed by serial arithmetic dilution of the serum and bile to a volume of 0.8 c.c. with isotonic buffered phosphate solution (pH 7.4) which contained 0.01 per cent thymol. Bacterial antigen was added so that the total volume was 1.0 c.c. The agglutination test tubes were incubated at 37° C. for twenty-four hours and were then examined with a hand lens for evidence of agglutination. Where there was any doubt about agglutination being present, the test tubes were centrifuged and the sediment was resuspended in 1.0 c.c. of physiologic saline solution and re-examined. Simultaneous controls in which the serum and bile of uninfected animals were tested against each of the antigens were included with each experiment. Parallel determinations of agglutination of *B. coli*, and *Staphylococcus aureus* by the test sera and bile specimens were included in order to provide a control for nonspecific agglutination. The original strains of bacteria were obtained through the courtesy of the Department of Bacteriology of the University of Pennsylvania. The typhoid bacillus (Strain 219T) was known to have a low virulence.

The organisms were kept in stock culture on agar slants and in beef infusion broth (pH 7.4). Stock cultures were transferred every five to six weeks. Antigen was prepared from 250 c.c. of beef infusion broth in which the organisms had been cultivated for twenty-four hours at 37° C. After centrifuging, the supernatant clear fluid was decanted and the bacterial residue was washed twice with physiologic salt solution and was then resuspended in 25 per cent of the original volume with normal saline solution. The organisms were killed with

thymol (0.1 per cent), and after twenty-four hours in the refrigerator the bacterial antigen was tested for sterility.

The antigens were diluted to contain four to five million organisms per cubic centimeter. These antigens were discarded when spontaneous agglutination or contamination occurred. No antigen was used for more than fifteen days. Gram stains were performed daily on all antigens and cultures in use.

When the gall bladder was removed, it was opened and examined immediately. After fixation in formalin, histologic sections stained with hematoxylin-eosin and methylene blue were prepared.

### RESULTS

Typhoid cholecystitis was produced in 16 dogs in which the biliary tract appeared normal before the experimental infection. The animals showed very slight constitutional reaction to the infection and none of the animals died.

The gall-bladder bile was sterile prior to the induced infection. Blood cultures were sterile. The gall-bladder bile at the time of the second operation contained the typhoid bacillus in 12 of 14 animals (85 per cent) in which the bile was available for culture. The typhoid bacillus was found in the hepatic bile in 6 of 7 animals within eighteen days of the experimental infection, and in only 1 of 9 animals after eighteen days.

The gall bladders which were removed six to fourteen days after the infection presented the gross and microscopic picture of an acute inflammation, the most prominent features being mural edema and cellular exudation. The incidence of bacteria in the gall-bladder wall as seen in histologic section was highest in this stage. From fifteen to twenty-two days after the infection the gross and microscopic picture was that of a subsiding infection. Hyperplasia was present and there was an excess of lipoid in the epithelial cells. After twenty-two days the gall bladder showed a chronic cholecystitis with early to advanced fibrosis. The excised gall bladder always presented a gross and microscopic picture of acute or chronic infection varying in its histologic pattern in relation to the interval from the induced experimental infection to the time of cholecystectomy.

Table I shows the agglutinin values of the serum, gall-bladder, and hepatic biles obtained at different periods following experimental infection. Three animals (Nos. 21, 23, and 852) showed significant agglutinin levels in serum and gall-bladder bile even before infection. These are included in Table I in order that the relative significance of spontaneous immunity in the group may be assessed. Two of these were subjected to cholecystectomy six days after infection, and both showed a marked rise in titer of serum, with little change in the level of agglutinin in the bile. The mean values shown at the bottom of

TABLE I

DOG	BILE	DAY							
		1	4	6-7	8-10	12-14	15-18	19-22	23-28
21	Serum	200		800					
	Gall-bladder	80		40					
	Hepatic			20					
24	Serum	100		1600					
	Gall-bladder	80		160					
	Hepatic	0		80					
867	Serum	0		80		1000			
	Gall-bladder	0				20			
	Hepatic								
524	Serum	10		160		2000			
	Gall-bladder	0				80			
	Hepatic								
18	Serum		500		3200		80		
	Gall-bladder	0							
	Hepatic								
852	Serum	1600		3200			2000		
	Gall-bladder	480					320		
	Hepatic						80		
295	Serum	0				160	320		
	Gall-bladder	0					40		
	Hepatic								
296	Serum	50			320		{ 640		
	Gall-bladder	5					{ 640		
	Hepatic						40		
							10		
297	Serum	50					{ 320		
	Gall-bladder	0					{ 640		
	Hepatic						20		
							10		
308	Serum	0				160	320		
	Gall-bladder	0					-		
	Hepatic						10		
320	Serum	6			320		640	640	
	Gall-bladder	0						320	
	Hepatic							80	
319	Serum	6			320		320	160	
	Gall-bladder	2.5						40	
	Hepatic							10	
269	Serum	40	320				640	80	
	Gall-bladder	0						20	
	Hepatic							2.5	
298	Serum	6			320		640		160
	Gall-bladder	0							80
	Hepatic								10
31	Serum	20			320		1250		{ 160
	Gall-bladder	0							{ 160
	Hepatic								40
									{ 5
									{ 20
34	Serum	40			{ 2000				{ 320
	Gall-bladder				640				{ 320
	Hepatic								80
									{ 10
									{ 10
Average, ex- cluding No. 852	Serum	37.7	410	670	930	830	570	300	224
	Gall-bladder	11.2		100			15	123	66.6
	Hepatic			50		50	10.0	31	11

the table, while having no accurate mathematical significance, will indicate the trend of the agglutinin values obtained. One animal (No. 852) is excluded in this average in order to afford greater statistical accuracy. The serum agglutinin reached a peak between the seventh and tenth days, and by the twenty-eighth day had returned almost to the control level. The gall-bladder bile agglutinin tended to lag behind the serum titer and did not reach a peak until the end of the third week. The curve of agglutinin in hepatic bile followed rather closely the serum curve.

The parallel determinations of agglutination of *B. coli* and *Staphylococcus aureus* failed to show any significant fluctuations during the period of observation. There were minor and transient alterations in the agglutinating power of serum and bile against these organisms, but the contrast between these alterations and those obtained from *B. typhosus* was sufficiently great to establish the specificity of the antibody reaction in this type of infection.

In two instances small calculi were found attached to the gall-bladder wall. These calculi were hard, brittle, greenish black, and from 2 to 3 mm. in diameter. These were found in one dog eighteen days and in the other twenty-two days after the induced cholecystitis. Microscopic examination showed that many clumped bacilli resembling the typhoid bacillus were present in the calculi.

The gall-bladder bile of two other dogs contained foreign substances. In one animal the material was in the form of mucoid pellets which were translucent, grayish green, and about 3 mm. in diameter. In the other instance the bile contained a coarsely granular dark pigmented sediment.

#### DISCUSSION

Bacterial cholecystitis has been found to be due to an intramural and submucosal infection.<sup>4-7</sup> However, the importance of other factors in the production of cholecystitis and cholelithiasis, such as trauma and stasis, has been stressed. The significance of the factor of trauma which entered into the experiments here reported is difficult to evaluate.

The gall-bladder bile was sterile prior to the experimental infection. Cultures taken at the time of cholecystectomy were positive for the typhoid bacillus in 85 per cent of the animals. The gall bladders of all of the animals showed microscopic evidence of infection, including those with sterile bile. Clinically, it has been demonstrated that from 42 to 65 per cent of individuals who have cholecystitis have bacteria present in their bile.<sup>9, 10</sup> The absence of a positive culture does not necessarily rule out an infectious origin of the cholecystitis, the presence of the organisms being simply confirmatory evidence.

Culture of the hepatic bile revealed the typhoid bacillus to be present in every sample collected prior to eighteen days following the



experimental infection. After eighteen days the typhoid bacillus was found in only one instance (at twenty-six days). These results indicate that an associated cholangitis was present, a lesion which often accompanies cholecystitis.<sup>11</sup>

Upon microscopic examination of the excised gall bladders, the common findings were edema, fibrosis, and cellular infiltration of the wall, the degree of alteration from normal depending upon the interval which had been allowed to elapse since the initiation of the experimental infection. Significant changes were also present in the epithelium, including hyperplasia, hypertrophy, and an increase in the lipid content of the epithelial cells. These observations agree with those reported in the literature where both mural<sup>9</sup> and epithelial<sup>12</sup> changes have been shown to exist in various phases of cholecystitis.

The rise in the agglutinin titer in the serum in response to induced typhoid cholecystitis agrees with reports in the literature. The response in the serum to any antigen or infection is usually a typical one, but may be modified by a number of factors.<sup>13-18</sup>

It might be expected that the agglutinin which appears in serum will also appear in bile, just as it appears in other body fluids. Passive immunization with autiserum<sup>2</sup> as well as active immunization with vaccine<sup>19</sup> will augment the antibody content of both serum and bile. In these experiments a specific agglutinin was found in the serum after an experimental infection, and the same antibody was found in the hepatic bile and in the gall-bladder bile.

The typhoid agglutinin in the serum was always greater than the similar agglutinin in the hepatic bile. The agglutinin in the gall-bladder bile was always greater than the similar agglutinin in the hepatic bile. The experimental evidence available, however, does not show that a definite ratio exists. The relation of hepatic bile, gall-bladder bile, and serum agglutinin varied with agglutinin, with the animal, and with the mode of production of the antibody.<sup>2, 19</sup> It seems probable that the high levels of gall-bladder bile agglutinin found at about twenty-one days, in spite of reduced serum values, were due to improvement in the concentrating power of the gall bladder with subsidence of the acute infection.

Calcification present in the epithelium,<sup>22</sup> calculus-like pigmented sediment,<sup>5</sup> and mucous pellets<sup>20</sup> as observed in this experiment have also been reported with clinical and experimental infection. Since typhoid bacilli have been found within gallstones,<sup>1, 21</sup> it is of interest to have found bacilli present in the mural calcifications formed in these dogs after an induced infection and in the presence of bacterial agglutinin.

#### SUMMARY

1. Suspensions of an avirulent strain of typhoid bacillus were injected into the gall bladders of healthy dogs.

2. The typhoid bacillus was identified in the gall-bladder bile (85 per cent) at intervals of from six to twenty-seven days after the induced cholecystitis.

3. Cholangitis accompanied the induced infection until eighteen days after the onset.

4. Histopathologic examination of the gall bladder showed a varying picture. The usual findings of infection were present and mural edema and fibrosis accompanied normal or altered epithelium in which there was often an increase in lipoid content.

5. Coal dust pigmented detritus and mucous pellets were found in the gall-bladder bile.

6. Small stones were found in two instances in which clumped bacilli were present.

7. The induced cholecystitis produced the appearance of a specific agglutinin in the serum, in the gall-bladder bile, and in the hepatic bile.

8. The gall bladder concentrates the agglutinin in the hepatic bile, and the concentrating power of the gall bladder increases as the gall bladder recovers from infection.

In conclusion, the onset of a bacterial cholecystitis stimulated the appearance of a specific agglutinin in the serum, in the gall-bladder bile, and in the hepatic bile. In two instances stones were found to be present in the gall bladder.

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## INTESTINAL OBSTRUCTION CAUSED BY GALLSTONES

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THE rarest of all the reasonable ways in which the intestine may become obstructed is by gallstones. Gallstones, however, frequently reach the alimentary tract through the common bile duct and occasionally through a fistula between the gall bladder or bile passages and the intestines or stomach. In cases in which intestinal obstruction has been produced by gallstones, the stone or stones usually have passed through fistulas.

The estimation of the frequency of the occurrence of gallstone ileus is now practically impossible. Wagner found that 334 cases had been recorded in the literature prior to 1914. In 1925 Moore estimated that 400 cases had been recorded. At the Mayo Clinic we have observed 10 cases in which intestinal obstruction was proved to be the result of gallstones. In these cases the obstruction was produced in one of three ways: (1) The stone was too large to pass through the lumen of the intestine; (2) the stone produced intussusception; or (3) the stone became embedded in the wall of the intestine and closed its lumen. In all of these cases it is probable that the stone or stones were too large to pass through the lumen of the intestine and that the intussusception or the inflammatory mass was a secondary reaction.

Table I shows the clinical findings in the 10 cases. Eight of the 10 patients were women and 2 were men. Only 3 of the patients had had definite symptoms of chronic cholecystic disease. Two had had indefinite symptoms. The rest of the patients had not had symptoms which are ordinarily associated with chronic cholecystic disease.

Cases in which intestinal obstruction is the result of gallstones may be divided into two groups, depending on whether or not there have been symptoms of chronic cholecystic disease: (1) those in which the patients have had recurring attacks of intestinal obstruction prior to the onset of complete ileus, and (2) those in which the patients have apparently been in good health prior to the onset of ileus. Of the 10 cases in this series, 5 belonged to the first group and 5 belonged to the second group. In all of the cases the gallstones had passed through a perforation in the gall bladder. In some cases the cystic and common bile ducts possibly may dilate sufficiently to allow the passage of a stone that is large enough to produce an ileus, but we have not

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TABLE I

CLINICAL FINDINGS IN CASES OF INTESTINAL OBSTRUCTION BY GALLSTONES

CASE	AGE, YEARS, SEX	SYMPTOMS CHARACTERISTIC OF CHOLECYSTIC DISEASE	SYMPTOMS OF INTESTINAL OBSTRUCTION	SITUATION OF FISTULA BETWEEN BILE PASSAGES AND ALIMENTARY CANAL	SITUATION OF INTESTINAL OBSTRUCTION	STONES PRESENT IN BILE PASSAGES	DIAGNOSIS MADE AT
1	31 F	None	Definite	Gall bladder to duodenum and supra-renal gland	Duodenum	No	Necropsy
2	44 F	Indefinite	Recurring	Gall bladder to duodenum and pancreas	Duodenum	No	Operation
3	44 M	Definite	Recurring	Gall bladder to hepatic flexure of colon	Colon	Yes	Operation
4	49 M	None	Definite	Gall bladder to duodenum	Duodenum	No	Operation
5	58 F	None	Definite	Gall bladder to duodenum	Distal portion of ileum	No	Operation
6	64 F	Definite	Recurring	Gall bladder to duodenum	Indefinite; progressed distally	Yes	Operation
7	65 F	Indefinite	Recurring	Gall bladder to duodenum	Indefinite; progressed distally	Yes	Operation
8	70 F	Definite	Recurring	Gall bladder to duodenum	Small intestine	Yes	Operation*
9	74 F	None	Definite	Gall bladder to duodenum	Distal portion of ileum	Yes	Necropsy
10	76 F	None	Definite	Gall bladder to duodenum	Distal portion of ileum	Yes	Necropsy

\*Died after operation.

observed such a case. It is our opinion that a gallstone that is large enough to cause intestinal obstruction usually reaches the intestine in only one way; that is, through a cholecystoenteric fistula. The fistula may not remain patent. At the time of operation or necropsy, the only evidence of a fistula frequently is the presence of adhesions.

Two of the 4 cases in which the obstruction was situated in the terminal portion of the ileum are of interest. In each of these cases the stone had passed distally for some distance but finally had to be removed. During the passage of the stones distally, the intensity of the symptoms of intestinal obstruction had slowly decreased.

If perforation of the gall bladder would permit the discharge of all the stones into the intestine, such an occurrence might not be a great catastrophe. However, perforation of the gall bladder and the subsequent formation of a cholecystoenteric fistula do not always empty the gall bladder and bile ducts of stones. In 6 of the 10 cases stones were still present in the gall bladder or bile passages when the patients were operated on or came to necropsy.

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The estimation of the frequency of the occurrence of gallstone ileus is now practically impossible. Wagner found that 334 cases had been recorded in the literature prior to 1914. In 1925 Moore estimated that 400 cases had been recorded. At the Mayo Clinic we have observed 10 cases in which intestinal obstruction was proved to be the result of gallstones. In these cases the obstruction was produced in one of three ways: (1) The stone was too large to pass through the lumen of the intestine; (2) the stone produced intussusception; or (3) the stone became embedded in the wall of the intestine and closed its lumen. In all of these cases it is probable that the stone or stones were too large to pass through the lumen of the intestine and that the intussusception or the inflammatory mass was a secondary reaction.

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estimate the frequency of such an unusual occurrence by the number of case histories to be obtained from a review of the literature.

When the intestine is obstructed by a gallstone, the obstruction usually is situated in the distal portion of the ileum. However, the obstruction may be situated at any narrowed portion of the alimentary tube.

For a correct diagnosis the clinician must depend on the surgeon or the post-mortem findings. The treatment, as in other cases of intestinal obstruction, is surgical except under very extraordinary circumstances.

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Intestinal obstruction by gallstones, as has been stated, in our experience has usually been secondary to the formation of a cholecystoenteric fistula which has resulted from the perforation of an inflamed gall bladder into the intestine. In no case had a peptic ulcer or carcinoma perforated into the gall bladder and allowed the stones to pass through the perforation and obstruct the intestine. A study of 176 cases of cholecystoenteric fistula disclosed that the perforation involved the following structures: the gall bladder and duodenum in 101 cases, the gall bladder and colon in 33 cases and the gall bladder and stomach in 7 cases. In 24 there were multiple perforations and stones were discharged into the abdominal cavity or into adjacent structures, and in 11 there were multiple perforations between the gall bladder, adjacent organs, and alimentary canal. From the foregoing data one can surmise that the site of intestinal obstruction by gallstones is usually in the small intestines. The clinical data in Table I show that in 1 of our cases the obstruction involved the small intestine.

Intestinal obstruction secondary to a chronic cholecystic disease followed by a perforation of the gall bladder may occur without the gallstones actually passing into the lumen of the intestine. In 2 cases (data not included in the table) the gall bladder had perforated onto the mesentery of the small intestine and the subsequent tumefaction and abscess formation were sufficient to produce the clinical signs and symptoms of intestinal obstruction. After appropriate surgical treatment, both of the patients recovered.

In cases in which intestinal obstruction is caused by gallstones, the cause of the obstruction rarely is suspected before operation or necropsy is performed. In the 10 cases in this series the diagnosis of the cause of the obstruction was made at operation or necropsy. There is nothing characteristic about intestinal obstruction that is caused by gallstones. In practically all cases of intestinal obstruction, the condition is preceded by minor and repeated symptoms that are indicative of varying degrees of obstruction. A history of chronic cholecystic disease is of no value. In many cases of intestinal obstruction, regardless of the cause, the patients have or have had chronic cholecystic disease.

#### COMMENT

Since the brilliant treatise on the clinical diagnosis and surgery of the gall bladder and bile passages by Courvoisier in 1890, many of the usual and unusual clinical observations concerning perforation and obstruction of the gall bladder and bile passages and intestines by gallstones have been recorded. Intestinal obstruction by a gallstone or gallstones has been reason enough to record the case history of such an illness. The recording of unusual case histories is commendable, provided physicians and surgeons do not lose perspective and try to

more than 70 years of age. Of this group of patients, 19 were men and 13 were women.

The ages of the 24 patients whose gall bladders had ruptured into the abdominal cavity varied as follows: One was less than 30 years of age; 1 was between 30 and 39 years; 2 were between 40 and 49 years; 10 were between 50 and 59 years; 8 were between 60 and 69 years; and 2 patients were in the eighth and ninth decades of life respectively. Fifteen of the patients were men and 9 were women.

The ages of the 7 patients who had fistulas between the gall bladder and stomach and the 11 who had multiple cholecystoenteric fistulas varied from 20 to 80 years. Two were less than 30 years of age; 2 were between 30 and 39 years; 5 were between 40 and 49 years; 3 were between 50 and 59 years; 4 were between 60 and 69 years; 1 was between 70 and 79 years; and 1 had passed his eightieth year. Of the 18 patients, 10 were women and 8 were men.

It is usually stated that in cases of chronic cholecystic disease the ratio of women to men is about 2:1. However, in this series of cases there were 103 women and 73 men. We believe that the increased number of women who have cholecystic fistulas can be accounted for by the usual preponderance of chronic cholecystic disease among women. There was nothing unusual in the age distribution in any of the groups or in the total number of cases. The greatest incidence of cholecystic fistulas was in the seventh decade of life.

The clinical history of the patients who had cholecystoduodenal fistulas was no different than the history obtained in cases of ordinary uncomplicated chronic cholecystic disease.

In 11 of the cases of cholecystoduodenal fistula the clinical histories were not definite. There had been periods during which the symptoms had been rather typical of chronic cholecystic disease which had subsided. Following these periods the illness had been characterized by chills and a low grade fever. There had not been very much abdominal distress. The symptoms of the 11 patients, however, were no different from the symptoms in the cases in which a subacute cholangitis developed during the course of chronic cholecystic disease.

Owing to the close proximity of the gall bladder and the colon, the colon is frequently perforated by a diseased gall bladder. When there is a cholecystocolic fistula the symptoms of chronic cholecystic disease without a marked degree of cholangitis are changed to symptoms of definite cholangitis. Of the 32 patients who had cholecystocolic fistulas, 19 recently had lost from fifteen to forty pounds. Two also had had severe chills, high fever, and protracted diarrhea. In the rest of the cases the chills and fever had not been accompanied by diarrhea. Seven of the 32 patients who had cholecystocolic fistulas were not seriously ill.



## CHOLECYSTOENTERIC FISTULAS

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**I**N CASES in which gallstones are associated with repeated colics, it is reasonable to assume that the stones are often discharged through the bile passages into the intestine. If the stone can pass through the bile ducts and reach the intestine, no serious complication arises. It has been stated that stones thus discharged have caused intestinal obstruction. However, at the Mayo Clinic we have not observed a case in which intestinal obstruction resulted from stones thus discharged. The passage of gallstones through cholecystoenteric fistulas is not a common occurrence. It is the object of this paper to record 176 cases of cholecystoenteric fistula.

A cholecystoenteric fistula may be produced in one of three ways: (1) by perforation of the gall bladder and intestine by gallstones, (2) by perforation of the intestine and gall bladder by a peptic ulcer, and (3) by perforation of the intestine and gall bladder by a carcinoma. In none of the 176 cases recorded was the obstruction the result of a perforated ulcer or carcinoma. Therefore, we limit this report to fistulas which arose primarily from biliary disease.

In the 176 cases the situation of the fistula was as follows: between the gall bladder and duodenum in 101 cases, between the gall bladder and the colon in 33 cases, and between the gall bladder and the stomach in 7 cases. Multiple fistulas between the gall bladder and adjacent organs and alimentary tube were found in 11 cases. In 24 cases the gall bladder had ruptured and the stones had been discharged into the abdominal cavity.

The age of the 101 patients who had fistulas between the gall bladder and the duodenum varied; 3 of the patients were less than 40 years of age and 25 were between 40 and 49 years of age. The highest incidence was between the ages of 60 and 69 years. Only 8 patients were past 70 years of age. Seventy-one of the patients were women and 30 were men.

The ages of the 32 patients who had cholecystocolic fistulas were as follows: One patient was less than 30 years of age; 2 were between 30 and 37 years of age; 8 were between 40 and 49 years; 9 were between 50 and 59 years; 10 were between 60 and 69 years; and 2 were

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more than 70 years of age. Of this group of patients, 19 were men and 13 were women.

The ages of the 24 patients whose gall bladders had ruptured into the abdominal cavity varied as follows: One was less than 30 years of age; 1 was between 30 and 39 years; 2 were between 40 and 49 years; 10 were between 50 and 59 years; 8 were between 60 and 69 years; and 2 patients were in the eighth and ninth decades of life respectively. Fifteen of the patients were men and 9 were women.

The ages of the 7 patients who had fistulas between the gall bladder and stomach and the 11 who had multiple cholecystoenteric fistulas varied from 20 to 80 years. Two were less than 30 years of age; 2 were between 30 and 39 years; 5 were between 40 and 49 years; 3 were between 50 and 59 years; 4 were between 60 and 69 years; 1 was between 70 and 79 years; and 1 had passed his eightieth year. Of the 18 patients, 10 were women and 8 were men.

It is usually stated that in cases of chronic cholecystic disease the ratio of women to men is about 2:1. However, in this series of cases there were 103 women and 73 men. We believe that the increased number of women who have cholecystic fistulas can be accounted for by the usual preponderance of chronic cholecystic disease among women. There was nothing unusual in the age distribution in any of the groups or in the total number of cases. The greatest incidence of cholecystic fistulas was in the seventh decade of life.

The clinical history of the patients who had cholecystoduodenal fistulas was no different than the history obtained in cases of ordinary uncomplicated chronic cholecystic disease.

In 11 of the cases of cholecystoduodenal fistula the clinical histories were not definite. There had been periods during which the symptoms had been rather typical of chronic cholecystic disease which had subsided. Following these periods the illness had been characterized by chills and a low grade fever. There had not been very much abdominal distress. The symptoms of the 11 patients, however, were no different from the symptoms in the cases in which a subacute cholangitis developed during the course of chronic cholecystic disease.

Owing to the close proximity of the gall bladder and the colon, the colon is frequently perforated by a diseased gall bladder. When there is a cholecystocolic fistula the symptoms of chronic cholecystic disease without a marked degree of cholangitis are changed to symptoms of definite cholangitis. Of the 32 patients who had cholecystocolic fistulas, 19 recently had lost from fifteen to forty pounds. Two also had had severe chills, high fever, and protracted diarrhea. In the rest of the cases the chills and fever had not been accompanied by diarrhea. Seven of the 32 patients who had cholecystocolic fistulas were not seriously ill.

When the gall bladder becomes acutely inflamed and contains stones, it may perforate into the abdominal cavity. This occurred in 24 of the cases in this series. In such cases the patients usually give a history of chronic cholecystic disease. The perforation of the gall bladder into the abdominal cavity may be a very serious complication of chronic cholecystic disease. However, the perforation often occurs slowly and the abscess cavity containing the stones is completely walled off by the omentum and the complication is masked by the clinical syndrome of acute cholecystitis and probably cholangitis. In only 5 of the 24 cases had the gall bladder perforated and stones been discharged directly into the abdominal cavity. In 3 of the 24 cases the gall bladder had perforated into the mesentery. The mesenteric abscess thus produced had caused symptoms of intestinal obstruction.

Cholecystogastric fistulas usually do not produce any untoward symptoms. This fact is well known as a result of the frequency with which relief has been obtained by a surgical anastomosis of the gall bladder to the stomach in cases in which carcinoma is situated at the head of the pancreas.

It is important to remember that fistulas between the gall bladder and the alimentary tube or adjacent organs may not always occur singly. In 11 of the cases in this series there were multiple fistulas. In the 11 cases the fistulas were usually situated between the gall bladder and the duodenum and liver. A perforation of the gall bladder into the alimentary tube is apparently of less serious importance than is the perforation and discharge of the stones into the parenchyma of the liver or into adjacent structures. In the first place a communication between the gall bladder and intestine permits discharge of at least some of the gallstones into the intestines and permits some drainage. In the second place, when the gall bladder perforates into an adjacent organ, the formation of an abscess is inevitable.

#### COMMENT

The bizarre and unusual instances of perforation of the gall bladder and migration of gallstones may be recalled by stating that gallstones have been seen in the pelvis of the kidney, in a persistent urachus, in the urinary bladder, in ovarian cysts, in a pregnant uterus, in the precordial cavity, and in the bronchial tubes. Fortunately, however, most gallstones that are spontaneously discharged from the body are either vomited or passed in the feces. The presence of gallstones in vomitus or feces does not always indicate the presence of a fistula.

The diagnosis of a cholecystoenteric fistula usually cannot be made by the clinical history or physical examination. Occasionally, the fistula can be demonstrated by roentgenologic examination. The presence of a fistula does not necessarily mean that all the gallstones have

been discharged into the intestine. Patients who have had a cholecystoenteric fistula have been known to enjoy good health for a long time. However, patients who have chronic cholecystic disease frequently enjoy a comparative freedom of symptoms for a long time. In either case it is not safe to "observe" the patients, because a cholangitis and hepatitis frequently will develop, or the bile duct or the fistula will become obstructed, and the subsequent jaundice will turn a relatively safe surgical procedure into one that is difficult for the surgeon and particularly dangerous for the patient.

## LUDWIG'S ANGINA

### AN ANATOMICAL AND CLINICAL STUDY WITH REVIEW OF THE LITERATURE

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THE term Ludwig's angina has been of rather vague significance in the minds of most surgeons since the first definite description by Ludwig (1836). A variety of conditions have been described as Ludwig's angina until the term has largely lost its significance as a clinical entity. In fact, as early as 1892 there was serious debate as to whether its consideration as a clinical entity was justified or not. One of the most active champions for retention of the name and its recognition as an entity was Delorme (1892), while on the other side, equally as active, was Nelatón (1892).

There are records of neck infections preceding Ludwig's classic description, but most of these are vague and inconclusive. Pothergill's description of "putrid sore throat" (1769) resembles Ludwig's angina only slightly. Gregory (1822), on the other hand, described a case which was undoubtedly one of Ludwig's angina and quoted similar cases by James of Exeter, Kirkland, and Willis.

Ludwig himself (1836), after giving his case history, emphasized the following points: (1) the comparative slight inflammation of the throat itself; (2) the peculiar "woody" hardness of the cellular tissue, on which an impression cannot be made; (3) the hard swelling under the tongue and the swelling of the floor of the mouth on the inner border of the mandible; (4) the well-defined border of hard edema in the neck; and (5) the absence of infection in the regional lymph nodes.

This description has been quoted by several later investigators and yet some of them insisted that the primary spread from the floor of the mouth to the submaxillary fossa was by lymphatics, and the later spread, back to the floor of the mouth and inferiorly in the neck, by fascial planes (Thomas, 1908; Muekeston, 1928). This view probably was based on the observation that the first demonstrable swelling is often in the submaxillary triangle of one or both sides with later swelling of the floor of the mouth. However, the external evidence of swelling is hardly proof of the portal of entry or means of transmission. Furthermore, some cases show their first visible swelling in the floor of the mouth and, according to the findings of most investigators, including Ludwig, the lymph nodes are not involved in the process.

Davis (1906), Blassingame (1928), Ashhurst (1929), Dehart (1933), Berryhill (1933), and others insisted that the spread was from the floor

of the mouth to the submaxillary region of one or both sides by tissue planes and not by lymphatics. This view would seem to fit Ludwig's original description as well as the anatomic and clinical findings of later investigators.

If the term Ludwig's angina is to be retained, as it no doubt will, it should be used to refer to a specific clinical entity and not to a variety of conditions, similar only in minor points or in their end results. From a study of the literature in which I have reviewed eighty-six articles from 1769 to 1938, including the original article by Ludwig (1836), I feel that the term Ludwig's angina should be reserved to refer to those cases of infection starting in the floor of the mouth, usually from carious lower molar or bicuspid teeth, spreading to the submental and submaxillary triangles (submandibular space) by fascial planes, and causing serious symptoms from edema of the tongue and glottis, mediastinitis, or toxemia. This definition automatically rules out spread by lymphatics, though obviously a periadenitis may lead to secondary fascial plane infection. It also practically eliminates the throat, tonsils, and pharynx as the seat of the initial lesion. Infections in these structures spread by lymphatics, or form retropharyngeal or lateral pharyngeal abscesses, which in turn spread secondarily to the submandibular space and resemble Ludwig's angina in the later stages.

#### ANATOMY

In order to fully appreciate the pathologic anatomy of Ludwig's angina, one must be familiar with the normal anatomy of the head and neck. In a previous article, Holyoke and I (1938) have reviewed the literature and given our description of the fasciae and fascial spaces of the head, neck, and adjacent regions based on the study of 75 adult cadavers and 5 full-term fetuses by dissection, injection, and section methods. It may be desirable to review this description at this time.

*Layers of Fascia.*—The superficial fascia is a continuous sheet of fatty tissue extending from the head and neck into the regions of the thorax, shoulders, and axillae. In the neck it is a moderately loose layer containing the platysma muscle in its deep portion. In the face the superficial fascia is very adherent to the overlying skin and contains the muscles of expression in its deep portion.

*Superficial Layer of Deep Fascia:* This layer crosses the anterior triangle of the neck, splits to form the sheath of the sternocleidomastoid muscle, crosses the posterior triangle, splits to form the sheath of the trapezius muscle and finally attaches to the spines of the vertebrae in the midline posteriorly. In the midline anteriorly it splits to form the suprasternal space of Burns, its anterior and posterior leaflets attaching to the corresponding margins of the sternum. Lateral to the sternum, it is attached inferiorly to the clavicle, acromion, and spine of the scapula. A corresponding layer, the superficial layer of deep pectoral



digastric muscle, although the two layers may be easily separated. It also becomes attached to the sheaths of the stylohyoid and posterior belly of the digastric muscles, and then splits to form the capsule of the submaxillary salivary gland. This is a completely closed capsule which attaches superiorly by two slips to the superficial and deep margins of the body of the mandible. The anterior belly of the digastric, the mylohyoid, the geniohyoid, the genioglossus, and the hyoglossus have independent sheaths with bony attachments at the attachments of these muscles. (Figs. 1, 3, 5, 8.)

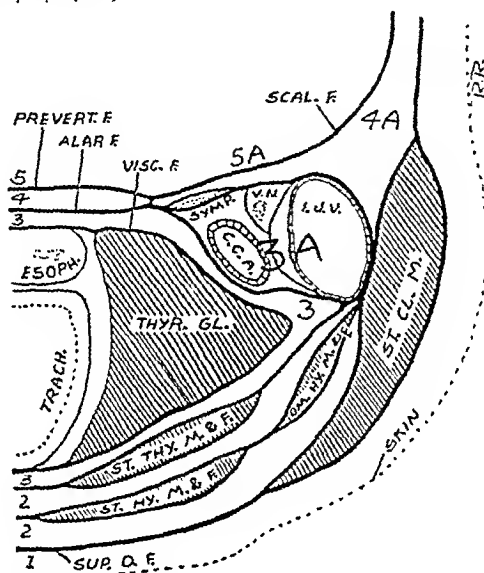


Fig. 2.—Diagrammatic drawing of fasciae of neck. Transverse section approximately at the level of the sixth cervical vertebra.

Between the angle of the jaw and the anterior border of the sternocleidomastoid muscle, the superficial layer of deep fascia splits to form the capsule of the parotid gland which in our experience is complete on all sides. From the body of the mandible, the superficial layer of deep fascia extends superiorly to form the sheath of the masseter muscle and attaches to the zygoma above. It then continues superiorly over the temporal muscle as the outer layer of deep temporal fascia. At the anterior and posterior borders of the masseter, it passes around the corresponding borders of the ramus of the mandible and becomes continuous with the sheaths of the pterygoid muscles, thus completing the walls of the masticator space (see below). (Figs. 3, 4, 8.)

*Middle Layer of Deep Fascia:* This consists of three subdivisions, the sternohyoid-omohyoid layer, the sternothyroid-thyrohyoid layer, and the visceral layer. The former is continuous across the midline anteriorly, forms the sheaths of the sternohyoid and omohyoid muscles, and attaches to the deep surface of the sternocleidomastoid sheath, where it forms a



pulley between the anterior and posterior bellies of the omohyoid muscle. Superiorly it is attached to the hyoid bone and, more laterally, to the overlying superficial layer of deep fascia and underlying sternothyroid-thyrohyoid layer along the superolateral border of the anterior belly of the omohyoid muscle. Likewise, in the posterior triangle, it is attached along the superolateral border of the posterior belly of the omohyoid muscle to the superficial layer of deep fascia. Inferiorly this layer is attached to the sternum, clavicle, and scapula. A corresponding layer, the deep layer of deep pectoral fascia, starts at the clavicle, splits to form the sheath of the subclavius muscle, becomes the costocoracoid membrane, splits to form the sheath of the pectoralis minor muscle, and becomes the suspensory ligament of the axilla which runs into the axillary fascia. (Figs. 1, 2, 6-8.)

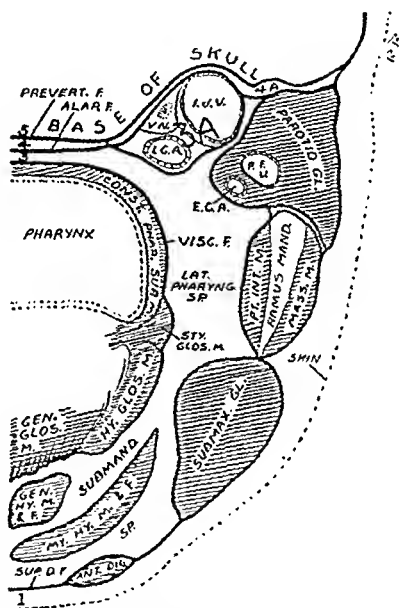


Fig. 3.—Diagrammatic drawing of fasciae of the head and neck. Oblique antero-posterior section showing the relation of the submandibular space to the lateral pharyngeal space and Spaces 3 and 4.

The sternothyroid-thyrohyoid layer crosses the midline anteriorly, splits to form the sheaths of the muscles indicated in the name, and laterally runs into the deep surface of the sternocleidomastoid sheath, fusing here with the carotid sheath. Inferiorly it attaches to the sternum and clavicle. Superiorly it attaches to the thyroid cartilage and hyoid bone; more laterally to the superficial layer of deep fascia and the sternohyoid-omohyoid layer superficially, and the carotid sheath deeply. (Figs. 1, 2, 6-8.)

The visceral fascia completely surrounds the thyroid gland, trachea, and esophagus. Superiorly, it extends to the base of the skull on the posterior side, and to the thyroid cartilage and hyoid bone on the ante-

rior and lateral sides. Inferiorly at the root of the neck it fuses with the alar fascia of the anterior wall of the carotid sheath and becomes continuous with the fibrous pericardium covering the heart and great vessels of the thorax. It also continues inferiorly as the covering of the thoracic portion of the trachea and esophagus. (Figs. 1-8.)

*Deep Layer of Deep Fascia:* There are two main subdivisions, the alar and prevertebral fasciae, including the continuations of the latter; eg., scalenus, transversalis, and Sibson's fasciae.

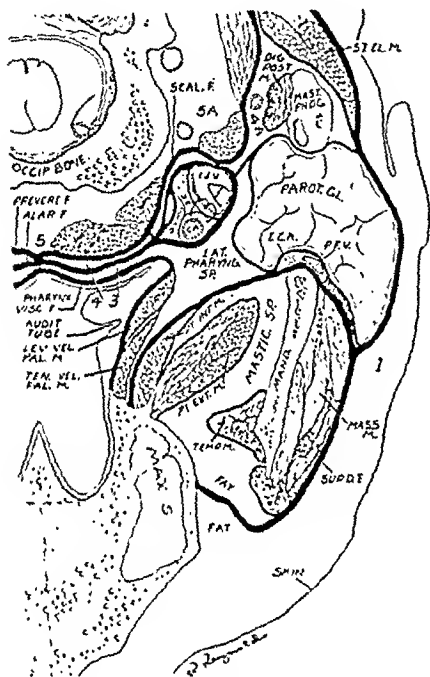


Fig. 4.

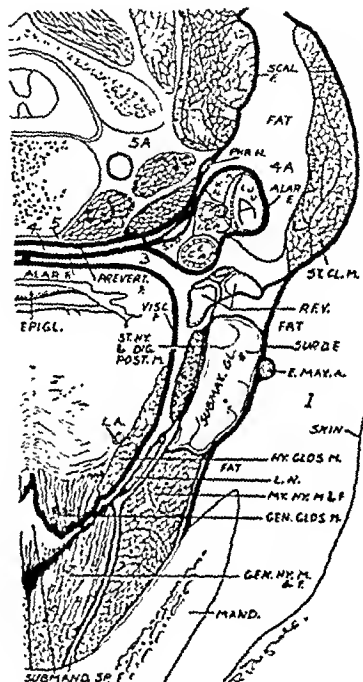


Fig. 5.

Fig. 4.—Transverse section of adult cadaver at level of hard palate. Superior view.

Fig. 5.—Transverse section of adult cadaver through the symphysis mandibular and the epiglottis. Superior view.

The alar fascia extends across the midline posterior to the pharynx, esophagus, and visceral fasciae, and fuses with the prevertebral fascia at the tips of the transverse processes to which both these layers are attached. It then passes anterolaterally to form the medial wall of the carotid sheath, fusing with the sternothyroid layer and the deep surface of the sternocleidomastoid sheath. It also forms the posterior and lateral walls of the carotid sheath, again fusing with the deep surface of the sternocleidomastoid sheath and thus forming a complete sheath of alar fascia, the carotid sheath. Posteriorly, between the transverse processes, the alar fascia extends from the base of the skull to about the level of the seventh cervical vertebra, where it becomes intimately fused with the visceral fascia. (Figs. 1-7.)

The prevertebral layer lies just anterior to the bodies of the vertebrae from the base of the skull to the coccyx. In the neck it extends laterally to the tips of the transverse processes where it is fused both to these processes and to the alar fascia. Lateral to the transverse processes, it becomes the scalenus fascia which forms the sheaths of the scaleni, splenius capitis, levator scapulae, and the other deep muscles of the back of the neck, and finally attaches to the spines of the vertebrae. Inferolaterally the scalenus fascia, after giving origin to the axillary sheath enclosing the axillary vessels and brachial plexus, attaches to the first and second ribs. In the thoracic and abdominal regions, the lateral extension of the prevertebral fascia becomes the extrapleuroperitoneal or transversalis fascia. Over the dome of the pleura, it is identical with the layer often described as Sibson's fascia. (Figs. 1-7.)

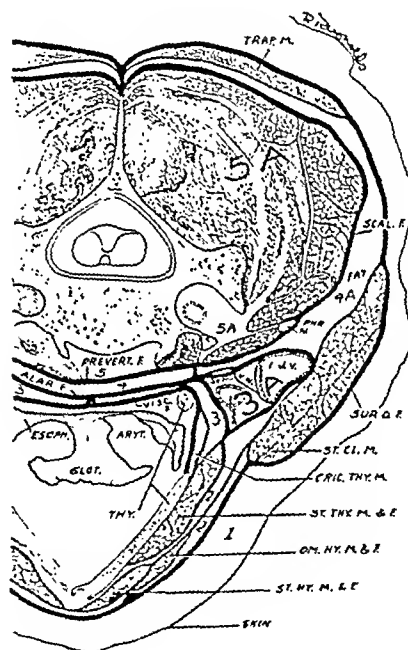


Fig. 6.—Transverse section of adult cadaver at the level of the thyroid cartilage. Superior view.

**Fascial Spaces.**—The superficial space (1) is the potential space between the skin and deep fascia; that is, within the superficial fascia. It is the seat of superficial cellulitis and is continuous from region to region; in this case, from head to neck and trunk. In the neck it may be subdivided into superficial and deep portions by the platysma muscle, both divisions being fairly loose and allowing rather large accumulations of fluids. (Figs. 1-5.)

**Deep Fascial Spaces:** These may be considered under two headings: those of the infrahyoid region and those of the suprahyoid region. For



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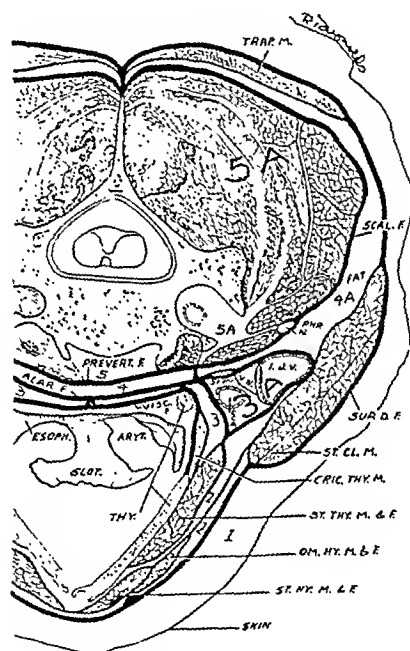


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mediastinum. It is because of the latter relationship that it is often called the "danger space." There was very little tendency for injected masses to spread beyond this space, the most common being into Space 4A. However, extension did occur from other spaces into this space, especially from Space 3. It is in this way that Ludwig's infection and retropharyngeal abscesses find their way into the posterior mediastinum. (Figs. 1-7.)

Space 4A is the potential space between the superficial layer of deep fascia and the scalenus fascia. In the subclavian triangle it lies between the sheath of the posterior belly of the omohyoid muscle and the scalenus fascia. This space is continuous with the axilla, but a rather dense fatty pad between the clavicle and the first rib makes this communication less free. (Figs. 2-7.)

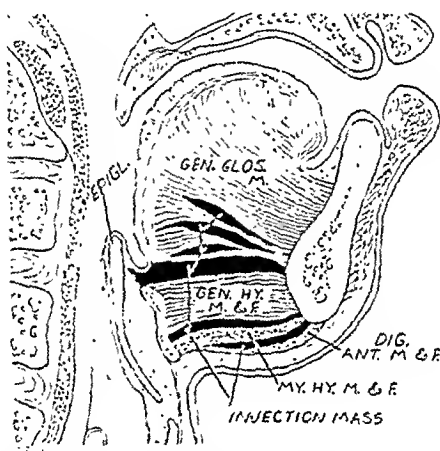


Fig. 9.—Diagrammatic drawing of median sagittal section showing the collection of infection masses between submental muscles and particularly the extension of the mass between the genioglossus and geniohyoid muscles toward the epiglottis.

Space 5 is the potential space between the prevertebral fascia and the bodies of the vertebrae. It extends from the base of the skull to the coccyx and is limited laterally by the attachment of the prevertebral fascia to the transverse processes. This is the space involved in tuberculous of the vertebral bodies, resulting in cold abscesses which extend inferiorly along muscles taking origin from the vertebral bodies (psoas abscess). There was very little tendency for injected masses to rupture through the walls of this space into Spaces 4, 4A, and 5A. (Figs. 1-7.)

Space 5A, posterior to the scalenus fascia, lies between the deep muscles of the back of the neck. Infections within it extend superiorly and inferiorly along these muscles, thus sometimes traveling great distances. (Figs. 2, 4-7.)

In the suprahyoid region are the masticator, temporal, parotid, lateral pharyngeal and submandibular spaces. The masticator space is bounded by the superficial layer of deep fascia which, after form-

Space 3 is the potential space between the visceral fascia on the one hand and the sternothyroid layer, carotid sheath, and alar fascia on the other. It thus has anterior, lateral, and posterior portions, all continuous. On the posterior side, it extends from the base of the skull to the level of the seventh cervical vertebra, where it is shut off by the close fusion of the visceral and alar layers. On the anterior side, it extends from the thyroid cartilage to the upper border of the arch of the aorta (fourth thoracic vertebra), where it is shut off by dense adhesions between the fibrous pericardium and the sternum. Laterally, this space is blind at the root of the neck where there are dense adhesions between the alar and visceral fasciae around the inferior thyroid arteries. Injected masses tended to remain localized within Space 3, but, when spread did occur, it was usually into Spaces 2, 4, and inferiorly into the superior mediastinum slightly lower than the normal limits of the space. This is of special importance in Ludwig's angina. (Figs. 1-7.)

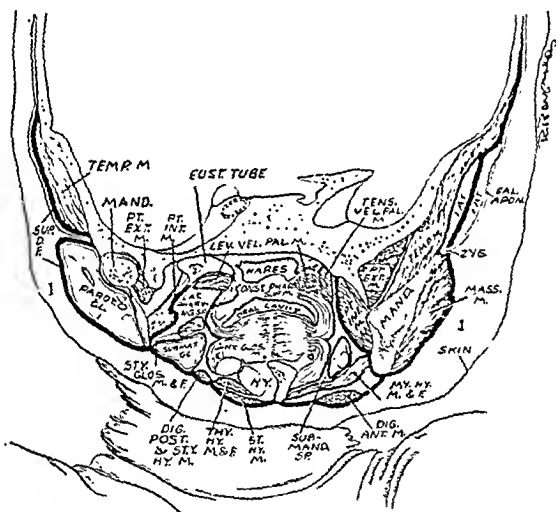


Fig. 8.—Frontal section of full term fetus through base of tongue and posterior nares. Anterior view.

Space 3A is the potential space within the carotid sheath. Primary injections into this space were usually limited closely to the region of injection, but in some cases the masses extended as high as the hyoid bone and as low as the root of the neck, beyond which levels the close adherence of the sheath to the contained structures made further spread impossible. The space therefore bears little relation to infections of the head and neck except those associated with thrombosis within the internal jugular vein and with the lymph nodes lying within the sheath. (Figs. 2-7.)

Space 4, often referred to as the "danger space," is the loose areolar space between the alar and prevertebral fasciae. It is limited laterally where these layers fuse at the tips of the transverse processes. It extends superiorly to the base of the skull and inferiorly into the posterior

hyoglossus and superior pharyngeal constrictor muscles, the latter covered by visceral fascia. Thus, a group of potential spaces, all communicating, is established between the submental muscles, crossing the midline and extending deep to the capsule of the submaxillary salivary gland, superolaterally, to become continuous with the lateral pharyngeal space. This group of spaces, collectively making up the submandibular space, is limited inferiorly at the hyoid bone where the submental muscles and their sheaths attach; and inferolaterally at the inferior borders of the stylohyoid and posterior belly of the digastric muscles, the sheaths which are attached to the superficial layer of deep fascia superficially and the carotid sheath deeply. (Figs. 3, 5, 8.)

Injections made through the mucous membrane of the floor of the mouth anywhere from the midline anteriorly to the anterior tonsillar pillar posteriorly passed into the submandibular space. The more anterior injections first passed between the submental muscles and then spread laterally toward the lateral pharyngeal space deep to the submaxillary salivary gland. The more posterior injections passed into the lateral pharyngeal space more quickly. From the lateral pharyngeal space, the injections often passed into Space 3, from where they sometimes spread to the superior mediastinum or broke through the alar fascia and extended down Space 4 to the posterior mediastinum. A similar extension of infection is one of the causes of fatal outcome in Ludwig's angina. In addition, there was usually submucous extension within the floor of the mouth, forming, with sufficient pressure, a horse-shoe-shaped elevation around the base of the tongue and extending back as far as the tonsillar pillars, pharynx, and larynx. A similar spread of infection and the accompanying swelling give the basis for the anginal symptoms in Ludwig's angina, often sufficient to produce fatal suffocation. The commonest rupture through the walls of the submandibular space was through or around the submaxillary capsule to the superficial tissues (Space 1) of the neck and face. Deeper breaks occurred laterally into the sheath of the sternocleidomastoid muscle and inferiorly, through the attachment of the stylohyoid and digastric sheaths to the carotid sheath, into Spaces 2 and 3 along the sternothyroid and sternohyoid muscles. These extensions account for the swelling in Ludwig's angina extending to the clavicle and up over the face. A fairly common extension was between the genioglossus and geniohyoid muscles posteroinferiorly to the region of the epiglottis where the mass appeared submucously (Fig. 9). A similar spread of infection would certainly be an important cause of edema of the glottis which is often the cause of death in Ludwig's angina.

#### ETIOLOGY

The great majority of cases of true Ludwig's angina originates from carious teeth, the infection of which erodes through the thinnest portion of the mandible. Since this is on the anterior (labial) side for the front teeth and buccal side for the back teeth (molar and premolar), the localization is superficially at the gums for the former, but deeper in



ing the sheath of the masseter muscle, passes around the anterior and posterior borders of the ramus of the mandible and becomes continuous with the sheaths of the pterygoid muscles. The space thus contains the masseter muscle, the external and internal pterygoid muscles, and the ramus of the mandible. It is closed on all sides except superiorly, where it is in relation with the temporal space, deep to the deep temporal fascia. Injections into either space spread to the other and, under increased pressure, ruptured either superficially through the masseter sheath or deeply into the parotid space or lateral pharyngeal and submandibular spaces. The parotid space was found to be a completely closed space formed by a split of the superficial layer of deep fascia and occupied by the parotid gland, external carotid artery, and posterior facial vein. Injections into this space showed infiltration into the substance of the gland and ruptures through the capsule; superficially with subcutaneous collections and deeply with extensions into the masticator, lateral pharyngeal, and submandibular spaces. Such collections in the submandibular space could in the later stages resemble Ludwig's angina even though the original infection was far removed from the floor of the mouth. (Figs. 3, 4, 8.)

The lateral pharyngeal space is an important fascial space of the head which is bounded by the pharynx, medially; the styloid muscles and carotid sheath, posteriorly; the parotid gland, posterolaterally; the mandible, pterygoids, and masseter, anterolaterally; and the pterygomandibular raphe, anteriorly. Superiorly, it extends to the base of the skull and, inferiorly, it is shut off from the neck by the attachment of the submaxillary capsule to the sheaths of the stylohyoid and the posterior belly of the digastric muscles. Inferomedially, it communicates freely with the submandibular space deep to the submaxillary capsule. Posteromedially, it communicates with Space 3. Injections made through the palatine tonsil and lateral pharyngeal wall went directly into the lateral pharyngeal space. From here, the injected masses spread easily into Space 3 and, in some cases, ruptured through the alar fascia into "danger space" 4. Extension into the submandibular space took place freely. The lateral pharyngeal space is therefore infected from tonsillar abscesses, from retropharyngeal abscesses involving Space 3, and secondarily from the floor of the mouth through the submandibular space. Likewise, infections in this space may spread to the submandibular space and, in the later stages, resemble true Ludwig's angina. (Figs. 3-8.)

The submandibular space is most important in the consideration of Ludwig's angina. We have coined the term submandibular space to include the regions of the submental and submaxillary triangles lying between the mucous membrane of the floor of the mouth and the superficial layer of deep fascia over these regions. It thus encloses the sublingual and submaxillary salivary glands (the latter in a complete capsule), the genioglossus, geniohyoid, mylohyoid, and digastric (anterior belly) muscles. The floor or deep wall of this space is made up of the

bination of the two may be used. The midline incision is indicated in obvious collections in the submental region, but often it fails to drain adequately more laterally lying collections. The lateral incision is more effective in the majority of cases and may be well combined with the median incision. In any event, the opening must be carried deeply to the mucous membrane of the floor of the mouth. Little or no pus may be obtained but beneficial release of pressure will result, and pus may appear in the wound a little later. In the midline the incision passes between the submental muscles of each side—anterior belly of the digastric, mylohyoid, geniohyoid, and genioglossus—a separation being made laterally in each plane to drain that particular level. In the lateral incision the procedure must include the displacement or excision (Rehn, 1922; Lindsay, 1923-4; Colp, 1933; Ramsdell, 1934) of the submaxillary salivary gland, incision through the mylohyoid muscle, and separation of the muscle planes medially. A combination of sharp and blunt dissection is safest. (Figs. 1, 3, 5, 8.)

#### CASE REPORTS

CASE 1.—A. G. (University Hospital No. 54086), male, aged 17 years, was admitted with high temperature ( $105^{\circ}$  to  $106^{\circ}$  F.), rapid pulse (120 to 150), and delirium. Nine days previously he had suffered a severe chill followed by high fever which subsided two days later. His only complaint at this time was backache. The next day his temperature rose to  $104^{\circ}$  F. and he complained of pain in the left knee. Five days later he complained for the first time of toothache on the right side; his temperature rose to  $105^{\circ}$  F. and he became delirious. The day before entrance, six upper and lower right molar and bicuspid teeth were removed, the teeth being loose and described as being "just lifted right out."

Physical examination showed a well-developed young man, acutely ill and in a semicomatose state. There were six bleeding sockets of recently extracted teeth in the right lower and upper jaws. There was moderate swelling of the submaxillary triangle and some swelling over the left sternoclavicular joint.

Laboratory examination: Red blood cells, 4,650,000; Hgb., 84 per cent; and white blood cells, 24,650. Urine showed 2+ albumin. Blood culture positive for hemolytic *Staphylococcus aureus*.

Course: Patient was given a transfusion of 500 c.c. of blood and supportive treatment, but died day after admittance.

Autopsy: Osteomyelitis of right maxilla and mandible with extension by continuity to submandibular space, Space 3, and the superior mediastinum. Metastatic abscesses in left sternoclavicular joint, chest wall, and most of internal viscera.

Comment.—This case presents the picture of a rapidly spreading infection, starting in the lower right molar and bicuspid teeth, extending through the floor of the mouth by continuity to the submandibular space, from there rapidly into Space 3, and then inferiorly into the superior mediastinum. The rapidity of the spread and absence of an inflammatory wall were no doubt responsible for the absence of marked swelling of the floor of the mouth and of anginal symptoms. Meanwhile the infection invaded the blood stream and gave rise to numerous metastatic abscesses.

the sublingual tissues, related to the mandibular canal, for the latter (Moty, 1892; Novitzky, 1935). The result is a spreading cellulitis along the routes already described (Figs. 1-9). A similar infection may result from scratches and wounds of the mucous membrane of the floor of the mouth, allowing direct access of pathogenic bacteria. The latter are usually the common pyogenes, streptococci, and staphylococci, but other mouth inhabitants such as Vincent's organisms and the spirochete group may be primary or secondary invaders. The majority of cases of true Ludwig's angina occurs in adults. Those cases described as occurring in infants and children no doubt originate in the nose and throat, spread by lymphatics, and are not true cases of Ludwig's angina.

#### CLINICAL COURSE

Following a history of swelling of the gums about the lower molar teeth which may or may not be accompanied by pain, the patient develops a fever which may be preceded by a chill. The temperature may vary from 99 to 105° F. An external swelling soon appears. This at first involves only the submaxillary triangle on that side or may start in the midline in the submental region; but, if not treated promptly, it soon spreads across the midline to the other side, superiorly over the face, and inferiorly to the sternum and clavicle. The submaxillary and submental swelling is characteristically "woody" hard, indicating the presence of deep inflammatory reaction under pressure, with or without free pus. The extensions superiorly and inferiorly may be superficial or deep according to the points of rupture through the walls of the submandibular space. The patient experiences difficulty in opening the mouth. The floor of the mouth becomes swollen and indurated; the tongue becomes swollen and elevated so as to touch the roof of the mouth and block the fauces. The respirations may become difficult and labored. If no relief is obtained, death results from suffocation due to the swelling of the floor of the mouth and tongue, or edema of the glottis, or both; or from mediastinitis, the spread occurring from the submandibular space to the lateral pharyngeal space and then to Spaces 3, or 4, or both, as indicated above (Figs. 1-9). Death also may occur from septicemia or aspiration pneumonia.

There is considerable variation in the acuteness and virulence of these cases, some being very fulminating and rapidly fatal and others of less severity or relatively benign.

#### TREATMENT

The sheet anchor of treatment consists in early and adequate drainage. Since death usually results from suffocation due to pressure or from extension of the infection to the mediastinum, it is obvious that early and proper incision offers the best hope of relieving pressure and preventing extension of the infection. Incision may be made vertically in the midline, or transversely below the body of the mandible, or a com-

bination of the two may be used. The midline incision is indicated in obvious collections in the submental region, but often it fails to drain adequately more laterally lying collections. The lateral incision is more effective in the majority of cases and may be well combined with the median incision. In any event, the opening must be carried deeply to the mucous membrane of the floor of the mouth. Little or no pus may be obtained but beneficial release of pressure will result, and pus may appear in the wound a little later. In the midline the incision passes between the submental muscles of each side—anterior belly of the digastric, mylohyoid, geniohyoid, and genioglossus—a separation being made laterally in each plane to drain that particular level. In the lateral incision the procedure must include the displacement or excision (Rehn, 1922; Lindsay, 1923-4; Colp, 1933; Ramsdell, 1934) of the submaxillary salivary gland, incision through the mylohyoid muscle, and separation of the muscle planes medially. A combination of sharp and blunt dissection is safest. (Figs. 1, 3, 5, 8.)

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Comment.—This case presents the picture of a rapidly spreading infection, starting in the lower right molar and bicuspid teeth, extending through the floor of the mouth by continuity to the submandibular space, from there rapidly into Space 3, and then inferiorly into the superior mediastinum. The rapidity of the spread and absence of an inflammatory wall were no doubt responsible for the absence of marked swelling of the floor of the mouth and of anginal symptoms. Meanwhile the infection invaded the blood stream and gave rise to numerous metastatic abscesses.

CASE 2.—C. H. (University Hospital No. 31713 and No. 32160), male, aged 23 years, entered the hospital complaining of *painful swelling* under left side of lower jaw, inability to open his mouth, and fever. Illness began four weeks previously with a swelling below the angle of the lower jaw which was not painful during the first week, but which became progressively more painful until a few days before entrance when there was a sudden additional increase in pain and swelling. Since the onset, it had become more and more difficult for him to open his mouth.

Examination on entrance showed a swelling on the left side of the face and neck involving chiefly the submaxillary triangle, but extending over the body and ramus of the mandible superiorly and halfway to the clavicle inferiorly. The swelling was firm, indurated, and moderately tender. The jaw could not be opened. The temperature was 101° F., pulse 80, and respirations 22. The teeth could not be examined on account of inability to open the mouth, but patient gave history of long-standing tooth pathology.

Laboratory findings: White blood cells, 10,800, with 72 per cent polymorphonuclears. X-ray showed osteomyelitis of jaw below left second and third molar teeth.

Course and treatment: On the day after admission external incision was made through a small area of fluctuation in the submaxillary swelling and a rubber drain inserted. Free pus was obtained which showed *Staphylococcus aureus* on culture. Six days later three additional incisions were made in the neck for drainage. Eight days later the jaws were pried open and the lower left second and third molars were removed. One week later incisions were made over the ramus of the mandible and lower in the neck for drainage purposes. A few days later the patient was dismissed from the hospital, improved. He was readmitted to the hospital one week later and an incision was made over the ramus of the mandible from the ear to the level of the thyroid cartilage. No free pus was obtained. One month later an additional incision was made posterior to the previous one. A small amount of free pus was obtained. Final operation was done one week later with incision posterior to former incisions, wide exposure, and blunt dissection deeply. From this time on, patient made a gradual recovery and left the hospital with wounds almost healed three weeks after readmission.

*Comment.*—This case presents a picture of true Ludwig's angina of moderate virulence, starting, as usual, from carious lower molar teeth and extending to the submandibular space from the floor of the mouth. The infection broke through the deep fascia and spread superficially over the face and lower neck. It also spread posterosuperiorly to the lateral pharyngeal space. There was apparently no mediastinal involvement. There was the usual swelling in the floor of the mouth and difficulty in opening the jaw. The numerous operations are evidence of a failure to appreciate the anatomic spaces and tissues involved, and of the resulting insufficient and unwisely placed incisions for drainage, although recovery eventually ensued.

CASE 3.—E. A. (University Hospital No. 60437), male, aged 23 years, entered the hospital complaining of swelling and pain of the right lower jaw, of six weeks' duration. Patient had a cold six weeks before entrance, which was improving when his right jaw, neck, and face swelled suddenly, over night. There was progressive difficulty in opening the mouth. Two days previous to onset of the swelling, he had consulted his dentist on account of pain and swelling over a nonerupted lower right wisdom tooth. The dentist "seared" the gum with an electric needle. About two weeks later, the wisdom and first molar teeth (lower right) were extracted under ether anesthesia in a local hospital, and he was discharged after ten days with the

external swelling well down but the gum still swollen. There was some drainage from a small skin incision over the angle of the jaw, made at the time of extraction. The external swelling with associated pain returned three days after discharge from the hospital. The external wound margins were spread and the patient was sent to the University Hospital.

Examination on entrance showed a hard, indurated swelling of the right submaxillary region extending superiorly over the mandible and inferiorly to about the level of the thyroid cartilage. It was very tender. Thick, yellow pus could be expressed from the small incision over the angle of the jaw. Culture showed *Staphylococcus aureus*. Temperature was 100° F., pulse 92, and respirations 15.

Laboratory findings: White blood count 8,600 with 48 seg. and 30 staff. X-ray showed rarefaction, about 2 by 4 cm. in area, in the right side of the body of the mandible under the extracted molar teeth, with questionable sequestration.

Course and treatment: Two additional small incisions were made, one over the body of the mandible and the other below the body of the mandible. There was rather free drainage of pus with reduction in the swelling and pain. The temperature and pulse are now practically normal, but I doubt if the patient will avoid further surgery, in view of the sequestration and the small inadequate incisions.

*Comment.*—This is a rather typical history of Ludwig's angina of moderate virulence treated inadequately by small incisions, unwisely placed. The treatment has been sufficient to control the original acute symptoms and prevent dangerous spread to the mediastinum, but insufficient to give prompt and complete recovery.

CASE 4.—R. V. (University Hospital No. 56297), female, aged 21 years, entered the hospital complaining of swelling and pain of the right lower jaw, fever, and difficulty in swallowing. Two days previously she noted a painless swelling in the region of the lower right, third molar tooth. Her dentist refused to extract until the swelling subsided. The swelling then became very painful, and the patient experienced difficulty in opening the mouth and swallowing. The day before entrance she had a severe chill and rise in temperature.

Examination on entrance revealed an indurated, boardlike swelling over the right submaxillary region, which extended across the midline anteriorly, over the angle of the jaw to the ear superiorly, and to the clavicle inferiorly. The mouth could be opened just 1 or 2 cm., revealing a swollen floor and an elevation of the tongue. The throat could not be visualized. Temperature was 104° F., pulse 96, and respirations 22. X-ray showed an area of rarefaction about the right lower second and third molar teeth (the latter impacted).

Course and treatment: The first operation, performed the day after entrance, consisted of removal of the lower right second and third molar teeth with establishment of internal drainage, care being taken to prevent aspiration of blood and pus into the lungs. In the second operation, done four days later, a midline incision was made through the skin and superficial fascia and the deeper structures were separated with a hemostat down to the floor of the mouth, releasing thick, foul-smelling pus. The third operation was done two weeks later with incision transversely to the right and below the previous midline incision. No free pus was obtained. There was gradual reduction in temperature, swelling, and induration. Patient was dismissed fully recovered.

*Comment.*—The above case presents a rather typical case of Ludwig's angina treated adequately by internal and external drainage. The internal and midline external drainage was effective in reducing the swelling and causing a subsidence of the general symptoms, but the appear-

ance or persistence of an indurated area farther laterally made an additional lateral incision necessary. Although no free pus was obtained here, the result was to hasten the convalescence and final recovery.

#### SUMMARY AND CONCLUSIONS

1. Ludwig's angina is a clinical entity resulting from spread of infection from the floor of the mouth by fascial planes.

2. The spread from the floor of the mouth occurs into the submandibular space, deep to the superficial layer of deep cervical fascia. Further spread may take place by rupture through the walls of this space superficially into the face and lower neck (Space 1), or deeply into the neck (Spaces 2 and 3).

3. Extensions may occur from the submandibular space deep to the submaxillary gland capsule to the lateral pharyngeal space. From here, the infection may spread to Space 3 by direct continuity, or through the alar fascia to the danger Space 4. From Space 3 the infection may extend to the superior mediastinum and from Space 4 to the posterior mediastinum.

4. Death from Ludwig's angina occurs either from suffocation due to edema of the floor of the mouth, tongue, and glottis; or from mediastinitis due to spread through the above mentioned spaces. Septicemia and aspiration pneumonia may be terminal.

5. The usual foci are the lower molar or bicuspid teeth, although scratches or wounds in the mucous membrane of the floor of the mouth may be the portals of entry.

6. Streptococci and staphylococci are the commonest organisms responsible, but Vincent's organisms and the common spirochetal inhabitants of the mouth may be primary or secondary invaders.

7. Infections starting from the nose and throat may spread into the retropharyngeal and lateral pharyngeal spaces or may extend into the neck by lymphatics. They should not be classified as cases of true Ludwig's angina, although they may resemble it in their later manifestations.

8. The clinical characteristics of true Ludwig's angina include constitutional symptoms (chills, fever, etc.) and local findings. The latter consist of boardlike swelling of the neck centering about one or both submaxillary triangles and the submental triangle (submandibular space), elevation of the floor of the mouth and tongue, and difficulty in opening the mouth, speaking, and swallowing.

9. Treatment consists of adequate and proper surgical drainage, instituted as soon as the diagnosis is made.

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## THE SURGERY OF THE TEMPOROMANDIBULAR JOINT

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AS COMPARED with other joints in the body, the temporomandibular joint is in many ways unique. It is a small joint which is in constant use, is frequently traumatized, and, yet, on the whole, is subject to few pathologic lesions requiring surgical interference. The joint itself is a complicated one, owing to the fact that it contains an interarticular fibrocartilage which divides the joint cavity into two separate compartments (Fig. 1). In the upper joint a gliding movement occurs, while in the lower, the movement is of a hinge character. The interarticular disk is of great importance for it may be torn or dislocated as the result of trauma. The disk itself is a thin, oval plate of fibrocartilage, the fibrous tissue predominating to such extent that in many cases in which I have excised the disk no cartilage cells have been visible under the microscope.

The upper surface of the disk is concavoconvex from before backwards, to accommodate itself to the form of the articular fossa and articular eminence on the temporal bone. The under surface, which is concave, is moulded onto the rounded head of the mandible. The capsular ligament of the joint is adherent to the circumference of the disk and the upper part of the tendon of the external pterygoid muscle is attached to its anterior part. The attachment of the external pterygoid muscle is of practical importance, for in such cases of dislocation of the joint the interarticular disk follows the condyle of the mandible.

### DISLOCATION OF THE JOINT

Owing to the stability of the joint and its protection by the overlying temporal muscle, dislocation is uncommon. In an analysis of 38 cases of forward dislocation of the jaw seen during the last twenty years, it

TABLE I

CAUSATION	MEN	WOMEN	TOTAL
Boxing bouts	20	0	20
Dental extractions	5	4	9
Use of gag during anaesthesia	4	1	5
Laughing	0	1	1
Yawning	1	2	3
Total	30	8	38

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## DISPLACEMENT OF THE ARTICULAR DISK

This is an uncommon accident, but a much more difficult condition to treat than dislocation of the joint.

Displacement of the disk may be caused by a violent cough, sneeze, or yawn, especially when the pterygoid muscles are contracted, as occurs

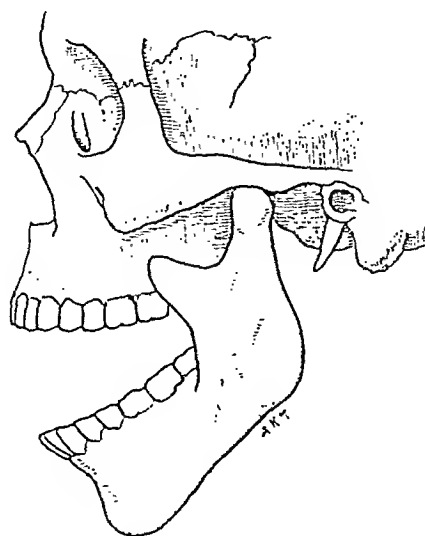


Fig. 2.—Forward dislocation of the mandible, showing the relation of the condyle to the articular eminence.

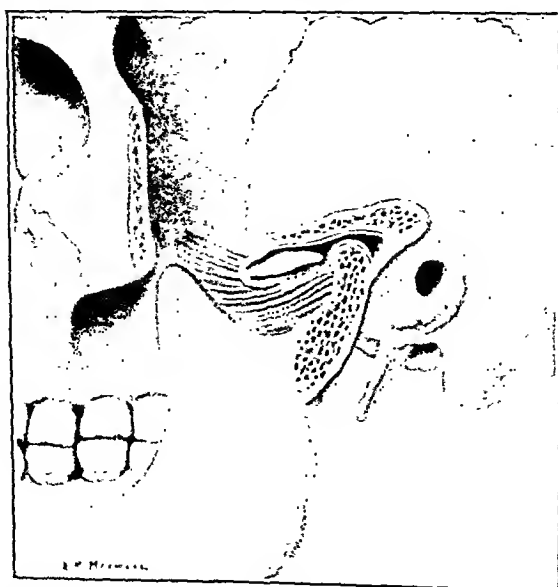


Fig. 3.—Section through the temporomandibular joint, showing the displaced articular disk. The action of the external pterygoid muscle is partly responsible for this, as can be seen in the drawing.

is interesting to note that only 2 developed recurrent dislocations and even these did not require any surgical intervention.

The causation of the dislocation is outlined in Table I.

This brings out the fact that boxing bouts, where a punch is directed to the point of the chin when the mouth is open, is the commonest cause of dislocation in men, while in women the commonest cause is dental extractions, especially where an attempt is made to elevate an unerupted third mandibular molar.

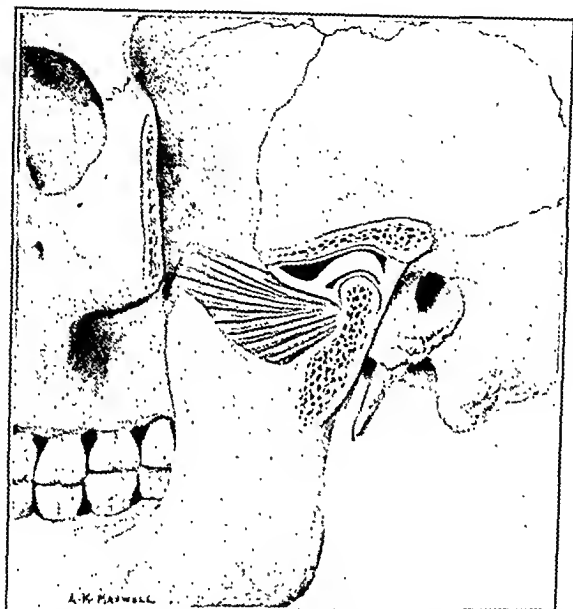


Fig. 1.—Section of the temporomandibular joint, showing the size and position of the articular disk.

The mechanism of forward dislocation is quite simple; the condyle of the mandible slips over the articular eminence (Fig. 2) into the zygomatic fossa of the temporal bone. The dislocation is usually bilateral, but may be unilateral, depending on the exciting cause; those due to dental extractions are mostly unilateral.

Reduction of the dislocation is easily carried out, and, as a rule, does not tend to recur owing to the fact that the muscles and periarticular structures are not weakened by the dislocation. Unreduced dislocations are rarely seen, and, when present for a long time, a false joint may result. In one case which came under observation, a gipsy woman, aged 76 years, had suffered from a dislocated jaw for twenty years, the dislocation being due to a bad dental extraction by another gipsy who used a pair of motor pliers to remove a lower molar tooth. The dislocation was unilateral and well-marked false joint had formed. The disability appeared slight, but talking was difficult.

displacement of the disk a synovitis is set up and this condition is to a certain extent responsible for the pain. Sometimes an x-ray picture of the joint may be of use in demonstrating the displaced disk (Figs. 4 and 5). Both temporomandibular joints should be x-rayed in order that a comparison may be made. On the side of the displacement a much larger joint space is seen when compared with the normal side. Reduction of the displacement is performed by exerting continual pressure behind the condyle of the jaw while the mouth is open. By this



Fig. 5.—X-ray of a case in which the articular disk has been displaced. Note the great increase in the joint space as compared with that shown in Fig. 4.

method the convex upper part of the condyle will be insinuated into the concave lower surface of the articular disk. Generally speaking, after a few minutes of continued pressure, the mouth is closed by gradually elevating the jaw. In some cases the disk slips back with quite an audible click, while in others the patient experiences a movement within the joint and is suddenly aware of the removal of all obstruction

when trying to prevent a cough, sneeze, or yawn. Occasionally, displacement may result from a blow on the jaw when the mouth is open, the trauma not being of sufficient force to cause dislocation of the condyle over the articular eminence of the temporal bone.



FIG. 4.—X-ray of a normal temporomandibular joint.

The posterior thinned-out part of the disk becomes detached from the capsule, which permits it to be drawn forward and inward by the external pterygoid muscle, and, as the mouth closes by elevation of the jaw, the disk of cartilage becomes severely crushed between the condyle and the glenoid fossa of the temporal bone (Fig. 3). The symptoms which result from such a displacement are quite characteristic. In some cases the patients volunteer the remark that they heard something snap in the ear. Sudden acute pain starting in the joint and referred to the pinna or the skin above it is a constant symptom. The auriculo-temporal nerve is responsible for the referred pain, as it not only supplies the joint but the pinna and the scalp in the temporal region as well. Excessive salivation is often quite a marked feature, owing to the stimulation of the nerve. Owing to the pain, the patient is unable to close the mouth and mastication is almost impossible. In all cases of

## ACUTE ARTHRITIS OF THE JOINT

This condition is relatively more common than is thought to be the case. It may follow scarlet fever, typhoid fever, gonorrhea, dento-alveolar abscess, acute parotitis, and rarely, acute mastoiditis, when inflammation spreads forward into the zygoma owing to the involvement of the air cells in this region. The surgeon is rarely called upon to deal with acute arthritis of the joint except in those cases in which suppuration takes place, and an incision is required to liberate pus. He is consulted, however, when ankylosis of the joint has occurred and the patient seeks relief from the disability therefrom.



Fig. 6.—Ankylosis of the temporomandibular joint of many years standing (Royal College of Surgeons Museum).

## ANKYLOSIS OF THE JOINT

When ankylosis occurs, the articular disk disappears and the whole surface of the glenoid fossa of the temporal bone and the upper surface of the condyle of the mandible become completely fixed (Fig. 6). It is not generally recognized how extensive and how firm is this bony ankylosis. On this account any relief or cure of the condition must be properly planned. Any attempt to divide the bony surfaces with a hammer and chisel will only result in an extensive fracture of the base of the skull with the possibility of meningitis as a further complication.

In a series of cases which have come under my supervision during the last twenty-five years in which a variety of surgical procedures have been performed, the ultimate results have been assessed, and now it may be said that crystallization of thought in treatment has occurred.



to free movement. To obtain this reduction quickly is a knack which can only be attained by experience; the surgeon may have to make several attempts before the disk is replaced to its normal position.

In those cases where the condition becomes chronic and repeated or almost continuous displacement occurs, there is a tendency for the disk to cause a "snapping" sound, every time the mouth is opened. This snapping is most noticeable during mastication and may become a source of great annoyance or embarrassment to a female patient or her friends. The psychologic effect of a snapping joint may be very marked, especially in females. They become introspective and nervous and are afraid to have meals in public.

It is the chronic cases, for the most part, which come under the surgeon's care, but not until every other form of treatment has been tried. Quite a number of these cases have been treated by osteopaths without any success. There is only one form of treatment which provides a permanent cure and that is excision of the articular disk, which cannot be looked upon as a very serious surgical procedure. The joint can best be exposed by means of a T-shaped incision, the edges of the wound being kept open by means of a small self-retaining retractor. On opening the joint capsule, the displaced articular disk is found in the anterior part of the joint. The disk is generally quite loose and can be removed entirely by cutting through its anterior connections with a knife. The capsule is then to be closed by two or three interrupted catgut sutures, and the skin approximated by a few silk-worm-gut sutures. A four-tail bandage is applied to the lower jaw and after full recovery from the anesthetic the patient is encouraged to open the mouth and so gain confidence that this movement can be undertaken without pain or snapping. The patient is allowed up on the second day and discharged from hospital at the end of a week, after the skin stitches have been removed. It might be thought that after excision of the articular disk the joint might not be stable and that the movements might be excessive with a tendency for forward dislocation of the jaw to take place, but this is definitely not the case. In some twenty cases recently examined at King's College Hospital in the follow-up clinic, the results were excellent both from the functional and anatomic standpoints, while all the patients were delighted with the result of the treatment. Some of the cases were operated upon more than fifteen years ago.

The whole profession realizes the excellent results which follow excision of the medial meniscus of the knee joint after it has been torn, but there seems to be a tendency for many physicians to remain sceptical with regard to excision of the articular disk of the temporomandibular joint, and to recommend their patients to continue with diathermy and other forms of treatment for years.

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In a series of cases which have come under my supervision during the last twenty-five years in which a variety of surgical procedures have been performed, the ultimate results have been assessed, and now it may be said that crystallization of thought in treatment has occurred.

It must be remembered that excision of the head of the mandible for ankylosis is quite an old procedure, being first performed by Professor Humphrey, of Cambridge, in 1856. Many successful cases have been reported from time to time, but how many bad results have never been published? That no stable operative technique has so far been established is proved by the fact that over a dozen different types of operation have been reported. The first difficulty that occurs is the size and shape of the incision, because there must of necessity be a limited approach owing to the important structures in the neighborhood of the facial nerve and on the medial side the internal maxillary artery (Fig. 7). A T-shaped incision over the joint gives the best exposure and

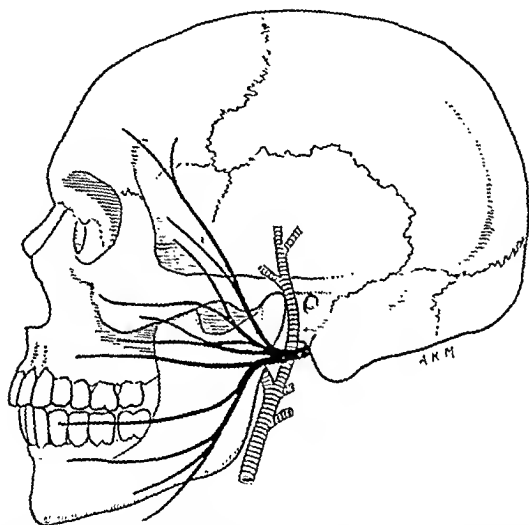


Fig. 7.—Drawing showing the relations of the facial nerve, the internal maxillary, and the superficial temporal artery to the temporomandibular joint.

does not damage any of the structures in the immediate neighborhood of the joint. The neck of the condyle is exposed and a fine Gigli saw is passed round it. The bone is then easily divided with a minimum of trauma. By means of a small pair of curved nibbling forceps, some of the bone constituting the condyle of the mandible is carefully removed. Next a dental burr is used to obliterate and flatten out the massive bone formation constituting the ankylosed joint. In my opinion it is the use of the dental bone burr which has established this operation as there is no likelihood of damage to the external auditory meatus or to the middle fossa of the skull.

When a conveniently large cavity has been made in the region of the joint, the exposed bony surfaces are rubbed with bone wax to prevent any oozing of blood and also to prevent any new formation of bone. Having tried a variety of different substances to cover the exposed surface of the neck of the condyle, I have come to the conclusion that the

patient's living tissues in the shape of muscle tissue is far the best. Celluloid, cargile membrane, and chromitized pig bladder have all been in vogue at one time or another, but the human body does not tolerate

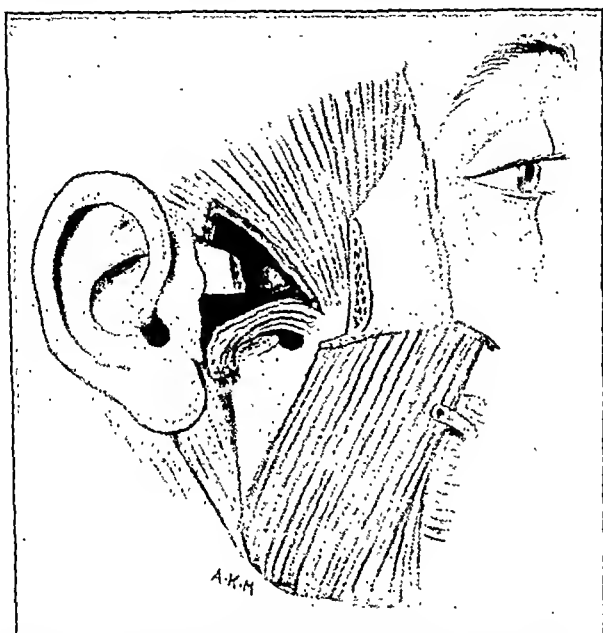


Fig. 8.—The use of a portion of the posterior part of the temporal muscle after excision of the temporomandibular joint.



Fig. 9.—The employment of some fibers of the masseter muscle after excision of the temporomandibular joint for ankylosis.

foreign tissue kindly. Simple procedures should always be advocated in place of difficult and complicating ones if they give the same results. It is quite easy to make use of a portion of the temporal muscle or a portion of the masseter muscle (Figs. 8 and 9), without affecting in the least the action and strength of the muscle itself.

The follow-up of these cases has been most instructive, for during the first year after operation there is no doubt that female patients make more rapid progress than male, and it is during this period that encouragement is required and some occasional diathermy treatment to the muscles in the neighborhood of the joint should be given. The results should not be assessed until at least six months after the operation when both surgeon and patient are quite pleased with the result. It must be remembered that quite often the ankylosis has been present for a long time and the muscles surrounding the joint have undergone atrophy from disuse. The re-education of these atrophied muscles takes a considerable time.

Age is no contraindication as some patients over the age of 80 years have been successfully operated upon. In infants, however, if they can be fed, it is better to postpone the operation until after 6 years of age, owing to the smallness of the joint.

In a few cases congenital ankylosis has been reported, but as Gladstone and I reported in 1923, antenatal defects of development appear to be the result of the same conditions which, in some subjects, may produce defect in growth, after as well as before birth. We believe that the defects in the growth of the face and lower jaw are usually associated etiologically with defective development of the brain.

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# THE TREATMENT OF THROMBOPHLEBITIS OF THE DEEP VEINS OF THE LOWER EXTREMITIES WITH INTERMITTENT VENOUS OCCLUSION

## A PRELIMINARY REPORT

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### INTRODUCTION

COLLENS and Wilensky<sup>1</sup> in 1936 reported the results of the use of intermittent venous occlusion in the treatment of certain types of peripheral vascular disease. This report, following soon after the work of Hermann<sup>2</sup> in the development of alternating positive and negative pressures for the treatment of the same type of disease, has further stimulated interest in the whole subject of therapy for vascular disorders. Thrombophlebitis, however, apparently has been excluded from consideration. We are unaware of any report of the effect of either intermittent venous occlusion or alternation of positive and negative pressures in the treatment of this condition. Indeed, the great majority of the advocates of both the above mentioned types of treatment have felt that the presence of thrombophlebitis constituted one of the contraindications to their use. The apparent reason for this is the fear that any increase in the venous pressure or mechanical massage of the affected extremity might increase the likelihood of the occurrence of pulmonary embolism. As far as is known there is no direct experimental or clinical evidence to support such a fear, at least as regards the intermittent venous occlusion treatment of Collens and Wilensky.<sup>1</sup>

Most of the problems inherent in the treatment of thrombophlebitis remain unsolved. In recent years the belief that cases of acute thrombophlebitis either occurring postoperatively or otherwise should not be subjected to too long a period of immobilization has been fairly generally accepted and probably with considerable improvement in the end results. Nevertheless convalescence is prolonged and the occurrence of the disabling sequelae of pain and chronic lymphedema appear frequently enough to merit the reporting of any new method of treatment which offers hope of still further improving the results in this condition.

### TECHNIQUE EMPLOYED

Four cases of thrombophlebitis of the lower extremities of recent origin and seven cases with a duration of two months or longer have

foreign tissue kindly. Simple procedures should always be advocated in place of difficult and complicating ones if they give the same results. It is quite easy to make use of a portion of the temporal muscle or a portion of the masseter muscle (Figs. 8 and 9), without affecting in the least the action and strength of the muscle itself.

The follow-up of these cases has been most instructive, for during the first year after operation there is no doubt that female patients make more rapid progress than male, and it is during this period that encouragement is required and some occasional diathermy treatment to the muscles in the neighborhood of the joint should be given. The results should not be assessed until at least six months after the operation when both surgeon and patient are quite pleased with the result. It must be remembered that quite often the ankylosis has been present for a long time and the muscles surrounding the joint have undergone atrophy from disuse. The re-education of these atrophied muscles takes a considerable time.

Age is no contraindication as some patients over the age of 80 years have been successfully operated upon. In infants, however, if they can be fed, it is better to postpone the operation until after 6 years of age, owing to the smallness of the joint.

In a few cases congenital ankylosis has been reported, but as Gladstone and I reported in 1923, antenatal defects of development appear to be the result of the same conditions which, in some subjects, may produce defect in growth, after as well as before birth. We believe that the defects in the growth of the face and lower jaw are usually associated etiologically with defective development of the brain.

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treatment was given during the course of four days. Fig. 1 shows the effect of treatment upon the pulse and temperature. The pain and tenderness in the legs subsided promptly with the fever. On the other hand, the edema, which at no time was more than moderate in amount, subsided somewhat more gradually. At the time of discharge from the hospital on Nov. 20 there was no edema of the legs when the patient was up out of bed for short intervals. The patient was last seen on Dec. 20, 1938. At that time the only residual from the thrombophlebitis was slight swelling of the ankles if the patient was up and about for several hours.

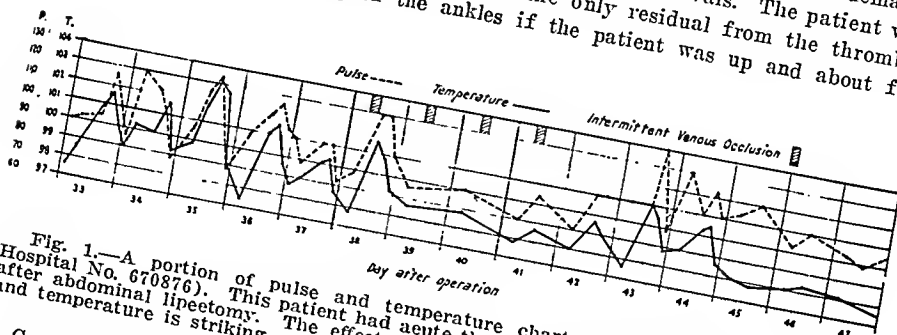


Fig. 1.—A portion of pulse and temperature chart of Mrs. O. C. (University Hospital No. 670876). This patient had acute thrombophlebitis of both legs five weeks after abdominal lipectomy. The effect of intermittent venous occlusion on the pulse and temperature is striking.

CASE 2.—Mr. M. D., University Hospital No. 647385. A 21-year-old farmer had his left lower leg removed Nov. 9, 1938, for a myxofibrosarcoma of the foot. A moderate postoperative reaction subsided by the third postoperative day. On Nov. 17 the patient's temperature rose to 99.6°. On the following day the temperature was 100.4° and the patient complained of pain and tenderness along the course of the femoral vessels in the stump of the left leg. By Nov. 22 the temperature had returned to normal, but the pain and tenderness remained. On Nov. 23 intermittent venous occlusion was begun. After five days, a total of 15 hours of treatment, there had been no return of the fever and all pain and tenderness had disappeared. A slight degree of edema which was noted before treatment was begun appeared to be unchanged.

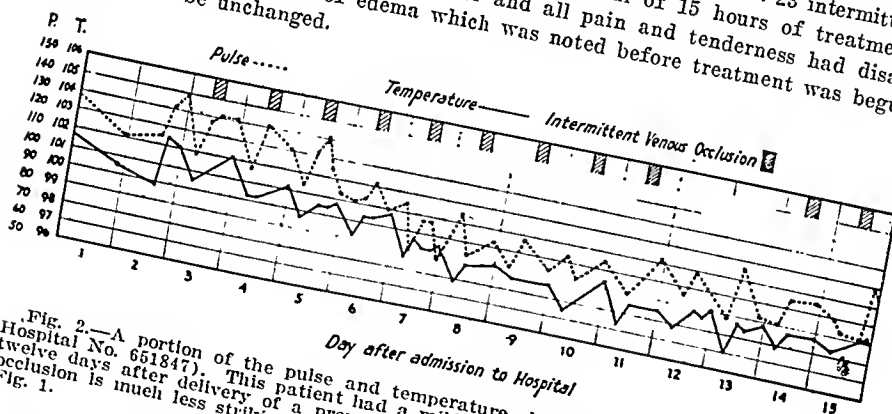


Fig. 2.—A portion of the pulse and temperature chart of Mrs. M. S. (University Hospital No. 651847). This patient had a mild acute thrombophlebitis of the left leg twelve days after delivery of a premature infant. The effect of intermittent venous occlusion is much less striking in this case than in the case of Mrs. O. C., shown in Fig. 1.

CASE 3.—Mrs. M. S., University Hospital No. 651847. A 32-year-old housewife was admitted to the hospital and delivered of a premature infant Nov. 14, 1938. On Nov. 26, after being out of bed for the first time, the patient noted pain in the medial portion of her left thigh extending from the groin down into the calf of her leg. The following day the entire left leg was swollen and painful. These symptoms and findings, combined with a daily rise of temperature to 100 to 101°



been treated with intermittent venous occlusion at the University of Minnesota Hospitals. The immediate results in this small series of unselected cases have been so striking that, despite the lack of adequate controls and follow-up study, they merit an early report. At the present time it must be admitted that no satisfactory rational explanation for the results obtained can be given. Certain experimental studies planned for the future should throw light on this subject.

After establishing a diagnosis of thrombophlebitis on the basis of history and physical examination, patients have been treated continuously for three to four hours a day five to six days a week with intermittent venous occlusion. During each period of treatment, patients were kept recumbent with the lower extremities slightly elevated. Venous occlusion was produced by wrapping a rubber bag 6 inches wide and 24 inches long around the mid thigh and holding it in place with a loosely applied elastic bandage. This bag was then inflated with air to 70 to 80 mm. Hg for two minutes. This period of inflation was followed by a period of deflation of equal length during which a slight negative pressure was maintained within the rubber bag. Thus, a four-minute cycle was used. These pressure and time relationships probably fall within the optimal range for the production of reactive hyperemia. Several types of apparatus, such as that described by Collens and Wilensky,<sup>1</sup> now can be purchased which will produce satisfactorily the alternating inflation and deflation automatically. A similar type of apparatus has been employed in the cases reported.

No other form of treatment has been employed in any of the reported cases. In three instances (Cases 1, 2, and 3) treatment was carried out with the patients hospitalized and in bed. The other eight cases have been ambulatory.

#### CASE SUMMARIES

##### *Acute Thrombophlebitis.*—

CASE 1.—Mrs. O. C., University Hospital No. 670867. A very obese, 40-year-old housewife was operated upon Oct. 3, 1938, for the removal of a large apron of fat on the anterior abdominal wall. The operative wound became infected and an atelectasis of the right lung developed. These complications had practically subsided when on Oct. 18 a sudden sharp pain occurred in the right chest. A diagnosis of pulmonary infarction was made. On Oct. 20 pain and swelling of the right leg with tenderness along the course of the femoral vessels were noted. Eight days later a similar condition was noted in the left leg. Both legs were placed in casts and elevated.

There had been a septic febrile temperature throughout the convalescence. This persisted with the development of the thrombophlebitis despite the fact that the wound infection had cleared up and the chest was normal to physical examination.

On Nov. 9, 1938, thirty-eight days after operation, treatment by means of intermittent venous occlusion of both legs was instituted. A total of 15.5 hours of

ment of the affected leg by elevation and heat relieved some of the swelling, but not the pain.

When this patient was seen on Oct. 14, 1938, she complained of persistence of the pain in the right leg which was greatly aggravated by walking. There was slight edema of the right ankle and lower leg as well as a subjective sensation of stiffness. The left lower extremity appeared normal.

Intermittent venous occlusion was begun on Oct. 17, 1938, and continued to Nov. 3. It was commenced again on Dec. 12 and discontinued on Dec. 23, a total of 88.5 hours. After 20 hours of treatment, marked subjective improvement was noted. Walking became easier, the stiffness of the joints was less pronounced, and the tissues about the right ankle were less indurated. At the end of the course of treatment, the patient could walk indefinitely without any difficulty and the slight edema noted at first had disappeared.

CASE 7.—Mr. D. S., University Hospital No. 673317. A 46-year-old farmer had influenza followed by thrombophlebitis of both legs in 1918. Massive edema of both lower extremities and extending up to the inguinal ligaments associated with local cyanosis and distended superficial veins ensued and persisted for twenty years. A continuous dull pain aggravated by walking or standing also developed.

When this patient was first seen on Oct. 28, 1938, many large tortuous superficial veins were present over the lower abdomen. The lower extremities from Poupart's ligament down to the dorsum of the feet were greatly swollen. The lower legs and feet were purplish blue in color and continually wet with perspiration. Many varicose veins were seen over both legs.

Intermittent venous occlusion was begun on both legs Oct. 29 and continued to Nov. 22, a total of 58.5 hours. After 15.5 hours of treatment, the patient remarked that his legs felt much better as far as the persistent pain was concerned. According to several observers, the edema had decreased a great deal. It is to be regretted that neither a photograph nor measurements of the legs were taken before treatment was begun. On Nov. 18, 1938, the edema had further decreased though the feet and lower legs remained cyanotic. At this time the patient stated that for the first time in twenty years he could cross his knees. Measurements of the circumference of the legs at this time were as follows:

	RIGHT LEG	LEFT LEG
Ankle	24.0 cm.	24.0 cm.
Calf	36.0 cm.	34.0 cm.
Lower thigh	48.0 cm.	44.0 cm.
Upper thigh	57.0 cm.	55.5 cm.

After 13 hours' more treatment and then seventeen days without treatment and without the support of elastic bandages, the legs were remeasured at the same levels as before:

	RIGHT LEG	LEFT LEG
Ankle	24.5 cm.	23.5 cm.
Calf	36.0 cm.	33.5 cm.
Lower thigh	43.5 cm.	42.0 cm.
Upper thigh	54.0 cm.	53.0 cm.

On Dec. 28, 1938, the patient died from a massive gastric hemorrhage. Post-mortem examination revealed a large gastric ulcer with an eroded artery in its base. The inferior vena cava and both common iliac veins were occluded by an old canalized thrombus.

CASE 8.—Mr. M. R., University Hospital No. 673806. A 33-year-old foundry-worker noted the onset of a painless swelling of the left lower leg in August, 1938. Five weeks in bed with leg elevated and the application of hot packs came

F., persisted until Dec. 1 when intermittent venous occlusion was begun. Treatments were given daily up to Dec. 30, 1938, a total of 81 hours.

After each period of treatment for the first three days this patient complained of an increased amount of pain. The pain and tenderness together with the fever then promptly disappeared and did not return. The edema of the limb remained the same despite the long period of treatment. The patient was discharged from the hospital Dec. 30, 1938, and has not been seen since.

CASE 4.—Mr. A. St. A., University Hospital No. 674405. A 56-year-old night-watchman in November, 1938, while convalescing in another hospital after an attack of coronary thrombosis, fell to the floor and bruised his right lower leg. During the succeeding two days the right lower leg became tender, swollen, and warmer than the opposite leg. These symptoms subsided within two weeks and the patient was discharged from the hospital. A week later a recurrence of these symptoms occurred. When this patient was first seen on Nov. 30, 1938, the right lower leg was swollen with an indurated edema. The muscles of the calf were tender to pressure. Over the thigh distended superficial veins could be seen. The entire extremity was warmer to the touch than the opposite.

Intermittent venous occlusion was begun on Dec. 2, 1938, and continued to Jan. 5, 1939. A total of 84 hours of treatment was given. No appreciable improvement was noted until after 26.5 hours of treatment had been given. The patient then noted that within the space of two days the pain, which had been present continually to some degree and in an increased amount when he walked, suddenly disappeared. After approximately 60 hours of treatment, the patient stated that his leg felt perfectly normal. The edema had decreased to the extent that the soft tissues of the lower leg became more pliable. The size of the affected leg, however, appeared to be unchanged. An additional 24 hours of treatment were given at the patient's own request.

### *Chronic Thrombophlebitis.*—

CASE 5.—Mr. W. A., University Hospital No. 642535. A 73-year-old retired farmer noted the sudden onset of dull pain in the left leg and thigh in July, 1938. Within 24 hours a similar pain was noted in the opposite leg and both lower extremities became swollen. Several weeks of rest in bed with the application of massive hot packs failed to relieve the condition.

When the patient was seen on Oct. 11, 1938, physical examination showed that both lower extremities were swollen with pitting edema. This edema was more indurated and of greater degree below the knees than above. Tenderness was minimal. There was no cyanosis of the feet or legs.

On Oct. 11, 1938, intermittent venous occlusion was begun in both legs for three to four hours a day and continued to Nov. 12. A total of 89 hours of treatment was given. After 12 hours of treatment, the patient stated that the pain in his legs had disappeared. After 40 hours of treatment, it was noted that the edema of the legs was less, the tissues were more pliable, and subjectively the legs were less stiff. This improvement continued during the remainder of the course of treatment. At the time of writing this patient has not returned for further observation.

CASE 6.—Mrs. M. McN., University Hospital No. 622335. A 64-year-old housewife with hypertensive heart disease was operated upon Aug. 5, 1938, for a recurrent nodular goiter with hyperthyroidism. Convalescence after a subtotal resection of the thyroid gland was uneventful until the day of her discharge when a feeling of fullness over the anterior medial aspect of the right thigh was noted shortly after leaving the hospital. Three hours later the leg pained quite severely and had begun to swell. On the following day she re-entered the hospital. Treat-

	RIGHT LEG	LEFT LEG
Ankle	20.0 cm.	24.0 cm.
Calf	35.0 cm.	42.0 cm.
Lower thigh	38.5 cm.	48.0 cm.
Upper thigh	50.0 cm.	55.5 cm.

On Dec. 14, 1938, the patient went hunting and walked for seven hours. There was no recurrence of the pain in the leg, but when next seen on Dec. 16 the circumference of the legs was as follows:

	RIGHT LEG	LEFT LEG
Ankle	21.0 cm.	27.0 cm.
Calf	36.0 cm.	45.0 cm.
Lower thigh	39.0 cm.	48.0 cm.
Upper thigh	51.0 cm.	55.5 cm.

When the patient was last seen on Jan. 6, 1939, there had been no further change in the size of the leg. The patient felt no discomfort or stiffness, however, if he was on his feet for as long as ten hours at a time.

Fig. 2 shows the change in appearance of the leg before and after treatment.

CASE 9.—Mrs. E. L., University Hospital No. 673974. A 38-year-old housewife had a spontaneous abortion in April, 1938. Three weeks later, pain and tenderness along the course of both femoral veins and a diffuse swelling of both legs up to the groin appeared. The usual treatment of elevation of the legs and application of heat was instituted and persisted in for several weeks. No improvement occurred except some decrease in the amount of swelling. Pain, severe enough to keep the patient confined to her bed at home, persisted up to Nov. 16, 1938, when she was admitted to the hospital.

Examination at that time showed the skin of both lower extremities to be dry and scaly. A moderate pitting edema was present in both legs. Along the course of the femoral vessels and over both calves there was extreme tenderness to pressure. On Nov. 17, 1938, intermittent venous occlusion was started on both legs and repeated daily until Dec. 1 when a total of 38.5 hours had been given. No appreciable change occurred in the amount of edema, but there was a complete relief of the pain. When discharged from the hospital on Dec. 2, 1938, she could be up for short periods without increase in the edema or recurrence of the pain.

CASE 10.—Mr. E. G., University Hospital No. 673389. A 60-year-old laborer who weighed 277 pounds and had hypertension and auricular fibrillation began to limp with the left leg in August, 1938. This leg soon thereafter became swollen and painful, especially when he walked. Rest in bed for seven weeks failed to improve the condition. During this time reddish colored spots which were tender to touch appeared over the calf. These areas would disappear after a few days, only to reappear in a new location.

When this patient was first seen on Nov. 18, 1938, there were no signs of cardiac decompensation. The left leg and thigh were markedly swollen from the level of the inguinal ligament downward. The foot and ankle were cyanotic and the skin over them tense and shiny. The calf of the lower leg and the medial and lateral aspects of the thigh were tender to firm pressure.

Intermittent venous occlusion was started Nov. 21, 1938, and continued daily until Dec. 2, 1938. The patient stated that after the first day's treatment (3.5 hours) his leg felt more limber. On Dec. 2, after 37.5 hours' treatment, he said that the pain in his thigh and leg had disappeared. Tenderness on pressure over the calf and thigh was no longer present. The edema, however, appeared to be unaffected.

## SURGERY

swelling largely to disappear. When the patient got up, however, the leg became painful and the swelling promptly returned and gradually progressed up the leg so that by October the lower portion of the thigh was swollen and by November the whole lower extremity below the inguinal ligament was involved. Pain was present throughout the leg on exercise and a certain stiffness of all the joints was present.



FIG. 3.—Mr. M. R. (University Hospital No. 673806). *A*, Indurated edema of the left leg before treatment by intermittent venous occlusion is marked; *B*, after 85.5 hours of treatment, the edema of the left leg is greatly reduced; this patient was ambulant throughout the whole course of treatment except during the periods of intermittent venous occlusion.

When the patient was first seen on Nov. 15, 1938, the right leg appeared normal. There was pitting edema of the entire left leg and thigh with areas of induration around the ankle. Measurements of the circumference of the leg were as follows:

	RIGHT LEG	LEFT LEG
Ankle	21.0 cm.	28.5 cm.
Calf	36.0 cm.	45.0 cm.
Lower thigh	40.0 cm.	48.0 cm.
Upper thigh	49.5 cm.	55.5 cm.

Intermittent venous occlusion was begun Nov. 15, 1938, and continued to Dec. 13, 1938, 85.5 hours being given. This patient noted no improvement during the first 24 hours of treatment, but then noted that the pain in his leg, which was increased when he walked, gradually disappeared. Soon thereafter the foot and ankle began to lose their stiffness. On Dec. 1, 1938, the edema of the foot and ankle had decreased to such an extent that the patient could put his shoe on for the first time in over three months. Improvement continued slowly from this time on to Dec. 13 when treatment was stopped. On this date measurements of the circumference of the leg at the same places as before were as follows:

TABLE I

	DIAGNOSIS	DURATION OF SYMPTOMS WHEN TREATMENT BEGUN	TOTAL HOURS OF TREATMENT	EFFECT OF TREATMENT ON:			
				TENDERNESS, PAIN AND DISCOMFORT	SIZE OF LEG	INDURATION OF EDEMATOUS AREAS	STIFFNESS OF JOINTS
Case 1, Mrs. O. C. (U. H. No. 670867)	Acute thrombophlebitis, both legs	19 days	15½ hr.	Relieved	Decreased	*	*
Case 2, Mr. M. D. (U. H. No. 647385)	Acute thrombophlebitis, left leg	5 days	15 hr.	Relieved	No change	*	*
Case 3, Mrs. M. S. (U. H. No. 651847)	Acute thrombophlebitis, left leg	5 days	81 hr.	Relieved	No change	*	*
Case 4, Mr. A. St. A. (U. H. No. 674405)	Acute thrombophlebitis, right leg	3 wk.	84 hr.	Relieved	No change	Decreased	*
Case 11, Mr. J. McA. (U. H. No. 661140)	Chronic thrombophlebitis, left leg	2 mo.	58½ hr.	Relieved	No change	Decreased	Relieved
Case 6, Mrs. M. Mc. N. (U. H. No. 622335)	Chronic thrombophlebitis, right leg	2 mo.	88½ hr.	Relieved	Decreased	Decreased	Relieved
Case 10, Mr. E. G. (U. H. No. 673389)	Chronic thrombophlebitis, left leg	3 mo.	37½ hr.	Relieved	No change	*	Relieved
Case 5, Mr. W. A. (U. H. No. 642335)	Chronic thrombophlebitis, both legs	3 mo.	89 hr.	Relieved	Decreased	Decreased	Relieved
Case 8, Mr. M. R. (U. H. No. 673806)	Chronic thrombophlebitis, left leg	3 mo.	85½ hr.	Relieved	Decreased	Decreased	Relieved
Case 9, Mrs. E. L. (U. H. No. 673974)	Chronic thrombophlebitis, both legs	6½ mo.	38½ hr.	Relieved	No change	*	No change
Case 7, Mr. D. S. (U. H. No. 673317)	Chronic thrombophlebitis, both legs	20 yr.	38½ hr.	Relieved	Decreased	Decreased	Relieved

\*These conditions were not present.

CASE 11.—Mr. J. MCA., University Hospital No. 661140. A 69-year-old retired farmer while walking to his barn on Oct. 1, 1938, noted the onset of dull burning pain throughout the whole left thigh. Within twenty-four hours the entire left lower extremity became swollen and the superficial veins more prominent than on the opposite leg.

When seen on Dec. 2, 1938, the lower leg was markedly swollen with edema. The foot was bluish in color. All the superficial veins were distended. The patient's chief complaints were a constant dull pain throughout both the left thigh and left lower leg. In addition, there was stiffness in the left foot and ankle.

Intermittent venous occlusion was begun on Dec. 5, 1938, and continued daily until Dec. 23, when 58.5 hours had been given. There was no decrease in the edema as indicated by measuring the circumference of the leg. The skin and subcutaneous tissue about the ankle became less indurated, however. The pain and stiffness complained of before treatment was started were no longer present when treatment was discontinued.

#### RESULTS OF TREATMENT

In Table I the results of the treatment of the eleven reported cases of thrombophlebitis of the lower extremities by intermittent venous occlusion are summarized.

It will be noted that in each of the reported cases the pain, discomfort, and tenderness present in the affected extremity when intermittent venous occlusion was begun were relieved during the course of treatment. In some instances this occurred after only a few hours of treatment, but in certain cases twenty or more hours were required to accomplish the same result. The effect of intermittent venous occlusion on the edema present and its secondary effects, such as induration and stiffness of joints, was variable and unpredictable. The edema in certain cases was unquestionably decreased a great deal, in others improved somewhat, and in still others unaffected. If improvement did occur, a certain sequel of events characteristically occurred. Induration, if present, decreased first. The skin and subcutaneous tissues became softer and more pliable. The subjective stiffness of the joints improved as the induration decreased. In certain cases improvement in the edema progressed no further than this, no actual decrease in the size of the leg being demonstrable.

There has been an opportunity to observe the effect of the treatment on fever due to acute thrombophlebitis in two cases. Fig. 1 shows the course of the pulse and temperature before, during and after a short course of treatment in the case of Mrs. O. C. (University Hospital No. 670867). In the case of Mrs. M. S. (University Hospital No. 651847), Fig. 2, a more gradual subsidence of fever and elevated pulse occurred over three days' time.

#### DISCUSSION

It is fully realized that further studies, more inclusive and better controlled, will have to be made before the full significance of the results reported in this paper can be evaluated correctly. It is our

TABLE I

DIAGNOSIS	DURATION OF SYMPTOMS WHEN TREATMENT BEGUN	TOTAL HOURS OF TREATMENT	EFFECT OF TREATMENT ON:			
			TENDERNESS, PAIN AND DISCOMFORT	SIZE OF LEG	INDURATION OF EDEMATOUS AREAS	STIFFNESS OF JOINTS
Case 1, Mrs. O. C. (U. H. No. 670867)	Acute thrombophlebitis, both legs	19 days	15½ hr.	Relieved	Decreased	*
Case 2, Mr. M. D. (U. H. No. 647385)	Acute thrombophlebitis, left leg	5 days	15 hr.	Relieved	No change	*
Case 3, Mrs. M. S. (U. H. No. 651847)	Acute thrombophlebitis, left leg	5 days	81 hr.	Relieved	No change	*
Case 4, Mr. A. St. A. (U. H. No. 674405)	Acute thrombophlebitis, right leg	3 wk.	84 hr.	Relieved	No change	*
Case 5, Mrs. M. Mc.A. (U. H. No. 661140)	Chronic thrombophlebitis, left leg	2 mo.	58½ hr.	Relieved	Decreased	*
Case 6, Mrs. M. Mc. N. (U. H. No. 622335)	Chronic thrombophlebitis, right leg	2 mo.	88½ hr.	Relieved	Decreased	*
Case 7, Mr. E. G. (U. H. No. 673389)	Chronic thrombophlebitis, left leg	3 mo.	37½ hr.	Relieved	Decreased	Relieved
Case 8, Mr. W. A. (U. H. No. 642535)	Chronic thrombophlebitis, both legs	3 mo.	89 hr.	Relieved	No change	Relieved
Case 9, Mrs. E. L. (U. H. No. 673806)	Chronic thrombophlebitis, left leg	3 mo.	85½ hr.	Relieved	Decreased	Relieved
Case 10, Mr. D. S. (U. H. No. 673974)	Chronic thrombophlebitis, both legs	6½ mo.	38½ hr.	Relieved	Decreased	Relieved
Case 11, Mr. J. Mc.A. (U. H. No. 673317)	Chronic thrombophlebitis, both legs	20 yr.	38½ hr.	Relieved	No change	No change
*These conditions were not present.						
			Decreased	Decreased	Decreased	Relieved



firm conviction, however, that intermittent venous occlusion in some way favorably influences the subjective symptoms and the disturbed circulation of limbs in which acute or chronic thrombophlebitis exists.

Very little is known concerning the pathologic physiology of thrombophlebitis. If three questions could be answered, the rational approach to an effective therapy would be placed on a much sounder basis. These questions are: What is the nature of the inflammatory process in the affected veins? What are the causes of the pain? What produces the edema?

Considerable confusion exists in the minds of clinicians as to the distinction which should be made between the pathologic process known as thrombosis and the clinical process known as thrombophlebitis. The histologic picture of an old thrombus may be indistinguishable from that of an old thrombophlebitis, yet the one may have given no clinical symptoms and the other may have given all the signs of an acute local inflammation. The study of thrombophlebitis from the viewpoint of bacteriology has been sadly neglected. The authors are unaware of any worthwhile investigation as to the incidence of bacteria in the thrombi of thrombophlebitis. The impression is gained, however, that in many cases the inflammatory process of thrombophlebitis develops, runs its course, and subsides in the absence of bacterial infection. Further investigations should be carried out to clarify this aspect of the problem.

Leriche<sup>5</sup> recently has set forth the idea that the pain associated with acute thrombophlebitis may be due to an associated spasm of blood vessels, both veins and arteries, in the affected limb. To relieve this vascular spasm he has in some instances infiltrated the lumbar sympathetic ganglia with novocain and in other cases removed these ganglia surgically. Such procedures have relieved much if not all of the pain in certain cases of both acute and chronic thrombophlebitis studied by Leriche. Ochsner<sup>6</sup> in 1938 reported satisfactory results in patients treated in this manner.

The importance of the venous obstruction present in thrombophlebitis in the production and maintenance of the edema is debatable. Experimentally it has been shown that simple ligation of the principal veins in an extremity will not produce a permanent edema. Homans<sup>3</sup> has further shown that in many cases of phlegmasia alba dolens there is an associated perivenous inflammation and infiltration of the perivenous tissue with a plastic exudate. He has stated that in these cases the persisting edema may be explained by a block of the trunk lymphatics which course through this inflammatory tissue. The experimental production of lymphedema in the hind legs of dogs by the injection of sclerosing substances into the trunk lymphatics reported by Homans, Drinker, and Field<sup>4</sup> lends substantial support to this idea. While such an explanation seems quite adequate in certain cases where

the existence of inflammation as judged by clinical signs seems incontrovertible, other writers, and even Homaus himself, have been reluctant to explain the edema in all cases of thrombophlebitis on this basis.

The work of dos Santos<sup>7</sup> in the delineation of the extent of the venous occlusion by roentgenologic examination after the injection of radio-opaque solutions into the peripheral veins offers a new approach to the subject of thrombophlebitis. He himself feels that this method offers a safe, early method of diagnosis, localizes the thrombus, offers a differential diagnosis of edemas and acute affections of the limbs, and gives evidence of the presence or absence of venous spasm. The exact interpretation of the roentgenograms obtained by dos Santos' technique is not easy. If the occlusion of the veins shown in some of his films is due to the presence of thrombi within them, the thrombotic process is much more extensive than is usually thought. It may be, however, that some portion of this occlusion is due to compression of the veins by the pressure of the edema in the surrounding tissues or to spasm of the smooth muscle in the walls of the veins.

On the basis of our present knowledge, the benefits from intermittent venous occlusion exhibited by the patients reported in this paper cannot be fully explained. It is well recognized that the occlusion of veins of an extremity will increase the venous pressure at points distal to the site of occlusion. Furthermore, increased venous pressure is always followed by increased flow of lymph. When venous occlusion is intermittent, however, another factor comes into consideration; namely, reactive hyperemia. None of these effects without further investigation can be asserted to be the effectual agent in our treatment of thrombophlebitis. It may be possible that the increased venous pressure due to occlusion dilates veins more or less occluded by extrinsic pressure, or that an increased flow of lymph dilates in a similar fashion compressed lymph channels. If Leriche is correct in his idea that pain in thrombophlebitis is due to vascular spasm, it may well be that the effects of reactive hyperemia relieve this spasm equally as well as interruption of the sympathetic nerve fibers does.

These various possibilities only emphasize the need of fundamental physiologic investigation of the disturbed vascular and lymphatic systems in thrombophlebitis. We propose to study additional cases by making venograms after the technique of dos Santos before and after treatment. In addition, changes in venous pressure and tissue tension are to be noted. It will have to be determined if an occluding pressure of 70 to 80 mm. Hg and a 4-minute cycle are within the optimal range for this condition. In the experimental laboratory the effect of intermittent external compression of the thigh of the dog on total blood flow, arterial pressure, and venous pressure, in the deep as well as superficial veins, will be studied.

A few clinical measurements already have been made. The venous pressures in the superficial veins of the lower leg during the course of distention and deflation of the occluding cuff have been measured in two cases. These measurements show that when the occluding cuff is distended to 70 to 72 mm. Hg (95 to 98 cm. H<sub>2</sub>O) the pressure in the superficial veins distal to the point of occlusion rises to 75 to 76 cm. H<sub>2</sub>O and remains at this level until deflation occurs at the end of the 2-minute period. During the 2-minute period in which the cuff is deflated, the venous pressure falls to 10 to 13 cm. of water.

Comparable results have been obtained in similar studies on two dogs. Rubber cuffs were wrapped loosely around the thighs and the changes in venous pressure in the femoral vein proximal to the cuff and in the external saphenous vein distal to the cuff have been followed as the cuff was distended to various pressures. These pressure variations are given in Table II.

TABLE II

	PRESSURE IN OCCLUDING CUFF	PRESSURE IN VEIN	PRESSURE IN FEMORAL VEIN
<i>Dog 1</i>	0 mm. Hg	23.5 cm. H <sub>2</sub> O	3.5 cm. H <sub>2</sub> O
	120 mm. Hg	79.0 cm. H <sub>2</sub> O	10.0 cm. H <sub>2</sub> O
	100 mm. Hg	75.5 cm. H <sub>2</sub> O	
	80 mm. Hg	53.5 cm. H <sub>2</sub> O	
	60 mm. Hg	42.5 cm. H <sub>2</sub> O	
	40 mm. Hg	28.0 cm. H <sub>2</sub> O	
	20 mm. Hg	18.0 cm. H <sub>2</sub> O	
	10 mm. Hg	17.0 cm. H <sub>2</sub> O	
	0 mm. Hg	21.0 cm. H <sub>2</sub> O	5.0 cm. H <sub>2</sub> O
<i>Dog 2</i>	0 mm. Hg	12.0 cm. H <sub>2</sub> O	3.5 cm. H <sub>2</sub> O
	100 mm. Hg	104.0 cm. H <sub>2</sub> O	1.5 cm. H <sub>2</sub> O
	80 mm. Hg	81.0 cm. H <sub>2</sub> O	
	50 mm. Hg	66.0 cm. H <sub>2</sub> O	
	40 mm. Hg	51.5 cm. H <sub>2</sub> O	
	30 mm. Hg	42.0 cm. H <sub>2</sub> O	
	10 mm. Hg	25.5 cm. H <sub>2</sub> O	
	0 mm. Hg	12.0 cm. H <sub>2</sub> O	4.0 cm. H <sub>2</sub> O

These few simple observations indicate the most obvious physiologic change produced by intermittent venous occlusion, but they explain not at all the reason for improvement in clinical cases. They lend support rather to the criticism which can be raised against this form of treatment; namely, that such a procedure may increase the likelihood of pulmonary infarction or embolism. Whether or not this is so cannot be settled by rationalization. In the eleven cases we have treated thus far, no signs of embolism have occurred.

## SUMMARY

Four cases of acute thrombophlebitis and seven cases of chronic thrombophlebitis of the lower extremities have been treated with intermittent venous occlusion. A rubber cuff 24 inches long and 6 inches wide was applied to the midportion of the thigh and intermit-

tently inflated to a pressure of 70 to 80 mm. Hg. A 4-minute cycle was used with two minutes of inflation and 2 minutes of deflation, continued for three to four hours a day. Pain, tenderness, and discomfort were relieved in each case. In some instances the edema was decreased. In two patients the venous pressure distal to the point of occlusion was measured to be 75 to 76 cm. H<sub>2</sub>O in the period of inflation and 10 to 13 cm. H<sub>2</sub>O in the period of deflation. Comparable venous pressure changes in normal dogs have been observed when a pressure cuff was applied to their thighs and distended.

Certain problems bearing on the treatment of thrombophlebitis which should be elucidated have been discussed.

#### CONCLUSIONS

1. Treatment of patients with acute and chronic thrombophlebitis of the lower extremities by means of intermittent venous occlusion relieved the pain, tenderness, and discomfort in eleven unselected cases. In some cases edema was decreased.

2. The distention of a rubber bag applied to the midthigh of patients with thrombophlebitis increases the pressure in the superficial veins of the lower leg to 75 to 76 cm. H<sub>2</sub>O if the bag is distended to 70 to 72 mm. Hg for 2 minutes. If the cuff is then deflated, the venous pressure falls to normal levels.

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## THE EFFECT OF INTRAVENOUS HYPERTONIC SUGAR SOLUTIONS ON TRAUMATIZED TISSUES\*

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THE intravenous administration of hypertonic solutions has been widely used clinically, especially in head injuries. So far as can be ascertained from the literature, this procedure is based on studies of the dehydrating effect of intravenous hypertonic solutions on normal tissues and no investigation of the results of intravenous hypertonic solutions on traumatized edematous tissues has been found.

### METHODS

Two tissues of healthy young male rabbits were subjected to trauma. In the first group trauma to one ear was produced by hitting with a felt-padded reflex hammer for a period of five minutes. The other ear was not traumatized in order to offer comparable normal tissues. In the second group the triceps and gastrocnemius muscles on one side were similarly traumatized under intraperitoneal sodium ethyl barbiturate anesthesia, the contralateral muscles not being traumatized for comparison. After a lapse of twenty-four hours, during which the animals were allowed food and water, control animals were sacrificed by a blow upon the occiput and the remaining animals were injected in the femoral vein with 8 c.c. per kg. of a 50 per cent solution of either sucrose or glucose. The solutions were freshly made and injected at body temperature at the rate of 5 c.c. per minute. The experimental animals were sacrificed at various intervals up to two hours after injection, being allowed no intake of water or food during the experimental period. The ears were amputated close to the head and the muscles were dissected and excised. Tissues were discarded if there was gross hemorrhage. Surplus blood was sponged away from the tissues with gauze. Fat was extracted from the minced muscle with ether. The wet weights of all the tissues were obtained and the tissues were dried to a constant weight in an oven at 105° C. and reweighed.

\*The material presented has been selected from a thesis submitted in partial fulfillment of the requirements for the degree of Master of Science, awarded June 13, 1938.

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## RESULTS

*Ears, 50 Per Cent Sucrose Injections (Table I).*—The values for the average percentage of water in the normal and traumatized ears dropped comparably at 30 minutes after injection. At 60 minutes after injection, the value for the normal ear remained unchanged, but that for the traumatized ear rose slightly above the preinjection level. At 120 minutes, the values in both instances were lower than the preinjection levels but higher than the values at the 30-minute, postinjection period. The maximum decreases in tissue fluid were less than twice the standard errors of the differences and are therefore without statistical significance.

TABLE I\*

FLUID CONTENT (PER CENT OF WET WEIGHT) OF NORMAL AND TRAUMATIZED RABBIT EARS AT VARIOUS INTERVALS AFTER INTRAVENOUS INJECTION OF 50% SUCROSE, 8 C.C. PER KG. OF BODY WEIGHT

EAR		SUCROSE 50%			
		CONTROL	PERIODS AFTER INJECTION		
		PER CENT	30 MIN.	60 MIN.	120 MIN.
			PER CENT	PER CENT	PER CENT
Normal	Min.	67.1	67.0	64.1	66.4
	Max.	73.5	71.2	72.7	72.5
	Ave.	70.7 ± 0.44 (18)	69.1 ± 0.77 (6)	69.1 ± 1.6 (6)	69.4 ± 0.42 (18)
Traumatized	Min.	68.3	71.8	66.2	67.4
	Max.	85.8	76.7	82.7	82.3
	Ave.	75.8 ± 1.05 (18)	74.1 ± 0.81 (6)	76.1 ± 3.15 (6)	74.6 ± 1.12 (18)

\*The figures in parentheses indicate the number of individual observations from which the averages were obtained. The apparent decreases in fluid content of both normal and traumatized ears at all intervals after injection are not significant as compared with the control levels.

*Muscle, 50 Per Cent Sucrose and 50 Per Cent Glucose Injections (Tables II and III).*—The changes in the average percentage of water in the normal and traumatized muscles roughly paralleled each other at the 5-, 15-, 30-, 60-, and 120-minute intervals after injection. The lowest water content of the muscle occurred 15 minutes after sucrose injection and 5 minutes after glucose injection. At these intervals the actual decreases were more than the standard errors of the differences and the results are therefore significant.

## DISCUSSION

It should be noted that the range between individual minimum and maximum values of tissue water in the controls is greater, even in the normal tissues, than the difference between the control average and the lowest average after injection. This comparison is exaggerated in the traumatized group as the result of obvious difficulty in the standardization of the amount of trauma. The fact that any dehydrating effect had been obtained therefore might be questioned were it not for the constancy with which injection was followed by a slight

TABLE II\*  
 FLUID CONTENT (PER CENT OF WET WEIGHT) OF NORMAL AND TRAUMATIZED RABBIT MUSCLES AT  
 INJECTION OF 50% SUCROSE, 8 C.C. PER KG. BODY WEIGHT  
 AT VARIOUS INTERVALS AFTER INTRAVENOUS

	MUSCLE	SUCROSE 50%					
		CONTROL		5 MIN.		15 MIN.	
		PER CENT	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT
Normal	Min. Max. Ave.	77.5 80.1 78.6 ± 0.24 (12)	76.5 77.5 77.1 ± 0.14 (12)	76.1 77.6 76.7 ± 0.18 (12)	76.2 79.1 77.2 ± 0.27 (12)	76.6 78.2 77.3 ± 0.18 (12)	77.1 80.6 78.2 ± 0.29 (12)
	Min. Max. Ave.	77.4 83.9 80.1 ± 0.60 (12)	76.1 80.9 78.5 ± 0.47 (12)	76.3 79.9 78.0 ± 0.32 (12)	76.9 82.2 79.1 ± 0.50 (12)	77.0 82.4 79.4 ± 0.62 (12)	77.4 81.4 79.4 ± 0.38 (12)
Traumatized	Min. Max. Ave.	77.4 83.9 80.1 ± 0.60 (12)	76.1 80.9 78.5 ± 0.47 (12)	76.3 79.9 78.0 ± 0.32 (12)	76.9 82.2 79.1 ± 0.50 (12)	77.0 82.4 79.4 ± 0.62 (12)	77.4 81.4 79.4 ± 0.38 (12)
	Min. Max. Ave.	77.4 83.9 80.1 ± 0.60 (12)	76.1 80.9 78.5 ± 0.47 (12)	76.3 79.9 78.0 ± 0.32 (12)	76.9 82.2 79.1 ± 0.50 (12)	77.0 82.4 79.4 ± 0.62 (12)	77.4 81.4 79.4 ± 0.38 (12)

\*The figures in parentheses indicate the number of individual observations from which the averages were obtained. The letter S signifies a statistically significant difference between the average value immediately above and the corresponding control.

TABLE III\*

FLUID CONTENT (PER CENT OF WET WEIGHT) OF NORMAL AND TRAUMATIZED RABBIT MUSCLES AT VARIOUS INTERVALS AFTER INTRAVENOUS INJECTION OF 50% GLUCOSE, 8 C.C. PER KG. BODY WEIGHT

		MUSCLE						GLUCOSE 50%					
		CONTROL	PERIODS AFTER INJECTION										
		PER CENT	5 MIN.	15 MIN.	30 MIN.	60 MIN.	120 MIN.		5 MIN.	15 MIN.	30 MIN.	60 MIN.	120 MIN.
Normal	Min.	77.5	74.6	76.0	75.5	76.5	76.7		74.6	76.0	75.5	76.5	76.7
	Max. Ave.	80.1 78.6 ± 0.24 (12)	77.3 76.1 ± 0.27 (12) S	78.8 77.1 ± 0.29 (12) S	77.3 76.2 ± 0.17 (12) S	79.1 77.7 ± 0.26 (12) S	77.7 77.1 ± 0.12 (12) S		77.3 76.1 ± 0.27 (12) S	78.8 77.1 ± 0.29 (12) S	77.3 76.2 ± 0.17 (12) S	79.1 77.7 ± 0.26 (12) S	77.7 77.1 ± 0.12 (12) S
Traumatized	Min.	77.4	75.5	77.0	78.2	76.9	78.0		75.5	77.0	78.2	76.9	78.0
	Max. Ave.	83.9 80.1 ± 0.60 (12)	80.5 77.9 ± 0.47 (12) S	80.7 78.9 ± 0.40 (12) S	81.4 79.7 ± 0.33 (12) S	81.6 79.8 ± 0.50 (12) S	81.6 79.9 ± 0.39 (12) S		80.5 77.9 ± 0.47 (12) S	80.7 78.9 ± 0.40 (12) S	81.4 79.7 ± 0.33 (12) S	81.6 79.8 ± 0.50 (12) S	81.6 79.9 ± 0.39 (12) S

\*The figures in parentheses indicate the number of individual observations from which the averages were obtained. The letter S signifies a statistically significant difference between the average value immediately above and the corresponding control.



decrease in water content of the tissues and for the statistical validity of the values for muscle. The apparent absolute dehydrating effect is a maximum in all tissues studied of only 2.5 per cent of wet weight.

Parallelism between the dehydration curves of normal and traumatized tissues is almost complete. It therefore appears that intravenous hypertonic sugar solutions in heavy dosage produce water withdrawal from normal or traumatized rabbit ears and muscles to so slight an extent as to be of no practical importance.

#### CONCLUSIONS

1. Withdrawal of water from the normal ear and muscle of the rabbit following the intravenous injection of hypertonic sugar solutions is slight and reaches its maximum within thirty minutes.

2. Dehydration of traumatized edematous tissues by the same means is parallel to that of normal tissues.

# THE TREATMENT OF ACUTE (NONTUBERCULOUS) EMPYEMA BY IRRIGATION AND NEGATIVE TENSION

## PRELIMINARY REPORT

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MANY methods have been advocated in the management of the acute (nontuberculous) empyemas between the time Hippocrates<sup>1</sup> suggested watchful waiting and that of drainage with contralateral pneumothorax recently suggested by Koster and his co-workers.<sup>2</sup> As early as 1889 Storch<sup>3</sup> advocated water suction aspiration in the treatment of empyemas. In 1898 Perthes<sup>4</sup> devised a negative tension apparatus for the evacuation of pus from the pleural cavity; in 1920 Moschowitz<sup>5</sup> showed that the maintenance of a negative tension in the pleural cavity helped evacuate the pus, and in 1934 Wangenstein<sup>6</sup> rediscovered the value of negative intrapleural tension in the treatment of empyema.

When we examine the results of all methods suggested for the treatment of empyemas and their modifications, we note that the mortality rate in the more commonly employed methods is more or less the same. Assuming therefore that therapy is instituted at the optimum time, if one seeks to reduce the mortality, he has but little choice between the various methods. However, in these same statistical reports we note that there is a wide difference in the morbidity. In the method which we are about to describe we have been able to reduce the morbidity at the Kings County Hospital from an average of 53 days of postoperative hospitalization to 37.3 days. In those cases in which negative tension drainage was employed all patients remained in the hospital until the sinus was healed and roentgenographic examination of the chest showed persistent clearing of the pleural cavity and complete expansion of the lung. Before this method was introduced, many of the patients who were treated by the conventional methods of intercostal drainage or rib resection drainage, were discharged with residual pneumothoraces or unhealed sinuses. So that, the post-operative period of hospitalization in the latter group of cases would be even greater had we subjected them to the same rigorous criteria as the cases we are reporting in this communication.

The proposed method is cognizant of the contributions of MacCallum<sup>7</sup> on the pathology of empyema, of Graham and Bell<sup>8</sup> on the relation of open pneumothorax to the treatment of empyema, and the work of

Anfreed<sup>9</sup> on the relation of the size of thoracotomy to the rate of the lung expansion. Regardless of the method employed, cure of any acute (nontuberculous) empyema requires (1) the evacuation of the pus at the optimum time, (2) the sterilization of the pleural cavity, (3) the complete expansion of the lung, and (4) the restitution to integrity of the thoracic cage. The present method does not present anything radically new in the treatment of empyema but rather emphasizes the principles governing the management of empyema based upon the pathologic process within the pleural cavity and, second, some advantages which may be obtained in the maintenance of a normal negative intrapleural tension. The acute nontuberculous empyemas may be subdivided into six groups; namely, (1) pneumococcic, (2) streptococcic, (3) pneumococcic and streptococcic, (4) staphylococcic, (5) anaerobic or facultative anaerobic, and (6) any combination of the foregoing. The latter three groups are distinct entities requiring special treatment not afforded by this method nor by the usual methods employed in the treatment of empyema, and are therefore omitted. The proposed method is particularly applicable to infections of the pleural cavity which are secondary to the usual pneumonias, pneumococcic and streptococcic.

*Pneumococcic empyema* is generally secondary to a pneumococcic pneumonia and is postpneumonic. Early in the course of the disease, the pus tends to become thick and is accompanied by a semiorganized fibrinous coagulum. The pus is relatively thick from the outset but tends to become thicker during the first two weeks. At the same time the coagulum becomes more organized. To attempt an early cure of such an empyema by means of simple aspiration or by means of an intercostal drainage must of necessity be doomed to failure more often than success. There is no doubt, however, that such empyemas have been cured by these methods, only at the expense of a prolonged morbidity. Those who have recognized the shortcomings of the above methods have suggested the use of the wide caliber tubes for drainage, with or without irrigation. Drainage under such conditions is more adequate, but not infrequently the tube becomes obstructed by the coagulum and the drainage impeded. If still larger tubes are used, i.e., one which will permit the coagulum to pass readily, it will also permit air to enter the pleural cavity at the same rate as it enters the trachea and therefore will inhibit the expansion of the lung. Such interferences with adequate drainage and expansion of the lung are obviated in the method about to be described, and in our cases have given satisfactory results.

#### METHOD

The patient is anesthetized in the usual manner. We prefer local paravertebral block anesthesia in the adult and general anesthesia in

the infant. The patient is postured either before the local anesthesia or after the general anesthesia, as the case may be, so that he rests on the contralateral side with the arm on the affected side drawn across the anterior chest. A rib is selected in the axillary region (usually the eighth rib), the interspace above which is the lowest point through which pus can be aspirated. About one and one-half inches are resected subperiosteally. This exposes the parietal pleura. A wet towel is then placed about the walls of the wound, leaving a small central area through which the pleura can be seen. A knife is then passed through the exposed pleura, and, as it is withdrawn, the towel is compressed. This prevents the flow of the pus into the wound. The pressure is gradually released and a suction tip is passed into the pleural cavity through the opening. As much of the pus is evacuated as is possible. The towel is then removed. The pleura is opened from one end of the cut rib to the other, leaving the suction tip in place. The pleural cavity is now aspirated under direct vision, removing the residual pus and coagulum. The larger pieces of coagulum may be removed with a dressing forceps. The pleural cavity is then flushed with warm normal saline solution and again aspirated. This irrigation and aspiration is continued until all the coagulum and pus are removed and the underlying lung shows signs of expansion. It is imperative that all the coagulum be removed. A soft rubber tube about one-half inch in diameter is prepared so that it contains a one-inch collar drawn to about one and one-half inches from the tip. This tube is then placed into the pleural cavity so that the tip points backwards and downwards towards the diaphragm. The pleura is then closed tightly about the tube with several interrupted black silk sutures. The intercostal muscles are approximated with interrupted chromic catgut sutures. The muscle sutures nearest the tube are so placed that they include the collar on the tube. This fixes the tube in place. The skin is then closed with interrupted black silk sutures and again the sutures nearest the tube are placed so that they include the collar. The pleural cavity is then filled with warm normal saline solution (through the tube), after which the tube is clamped with a hemostat. A collodion or rubber cement soaked gauze dressing or liquid adhesive is then applied to the skin over the wound and about the tube at the site of its entrance into the thorax. When dry this forms an airtight dressing. The patient is then returned to his bed and placed in the semi-orthopneic position as soon as feasible. The drainage tube is then connected to a glass Y-tube, the upper arm of which is attached to a suspended irrigating container and the lower arm to a glass subaqueous drainage tube, Fig. 1. The subaqueous tube rests on the bottom of a colorless glass bottle and about four inches below the surface of water in the bottle. This collecting bottle should be placed below the level of the bed, preferably on the floor at the patient's bedside. A

screw stopcock is then placed on the tube leading from the chest, proximal to the hemostat, closed tightly, and the hemostat removed. The irrigating bottle is filled with normal saline solution. When all the air in the system has been expelled, the rubber tube leading to the irrigating container is clamped with the hemostat, Fig. 1A. During the first three or four hours postoperatively the stopcock should be opened gradually, allowing a slow trickle of the pleural content. In about three hours the stopcock should be completely opened allowing a free communication between the pleural cavity and collecting bottle. In about six or eight hours the flow will stop spontaneously. At this time the stopcock may be removed. It will be noted that the respiratory excursions of the thorax are accompanied by fluctuations in the glass drainage tube. Thus, the intrapleural pressure will be expressed in the fluctuations within this tube. When the stopcock is first opened, the intrapleural pressure being positive, there will be no fluid level within this tube. As the pleural cavity rids itself of its contents, the intrapleural pressure becomes negative and the fluid level in the tube rises in response to the negative pressure within the pleural cavity. This pressure becomes increasingly negative until an equilibrium is established. The maximum negative pressure is reached usually within about twelve hours.

Irrigation of the pleural cavity is begun about eight hours postoperatively. The substance of the instructions to the patient or nurse is as follows:

The hemostat on the irrigating tube (Fig. 1A) is removed and placed on the drainage tube (Fig. 1B). This allows the irrigating solution to flow into the pleural cavity. The patient allows the fluid to enter the cavity until he feels a tightness in the chest. The hemostat is then replaced in its original position—Fig. 1A. This allows the pleural content to drain out into the collecting bottle. When the flow has ceased, the patient is turned toward the affected side and encouraged to cough. This helps expel the residual fluid. The irrigation is repeated every two or three hours.

After twenty-four hours of the above procedure, the tube originally inserted into the thorax is clamped proximal to the Y-tube and the connections thereto removed. A mercury manometer is connected to the upper arm of the Y-tube, and the negative pressure apparatus, shown in Fig. 2, is connected to the lower arm of the Y-tube. A Murphy drip tube is then placed in the siphon drainage system. A siphon drainage is established from Bottle 2 to the collecting bottle. The stopcock at C in Fig. 2 is then closed so as to allow only a slow drip through the Murphy tube. This creates a negative pressure which is transmitted to the pleural cavity and registered in the manometer. The siphonage should be so regulated that the intrapleural pressure approximates that within the normal pleural cavity.

With the patient in the semiorthopnoeic position, the pressure should be about  $-10$  mm. of mercury at the end of normal inspiration and  $-5$  mm. of mercury at the end of normal expiration. Once the desired pressure is reached it can be maintained by the slow drip of the siphonage at about five drops per minute, after which the apparatus works automatically. When Bottle 2 becomes empty, the tubing proximal to the Y-tube is clamped with a hemostat and filled with colored water. The siphonage is then reestablished and the pressure noted. When the manometric reading is the same as that before the tube was clamped off, the hemostat is removed. This least disturbs

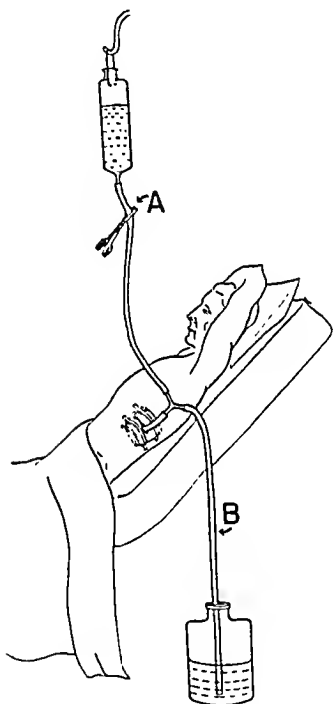


Fig. 1.

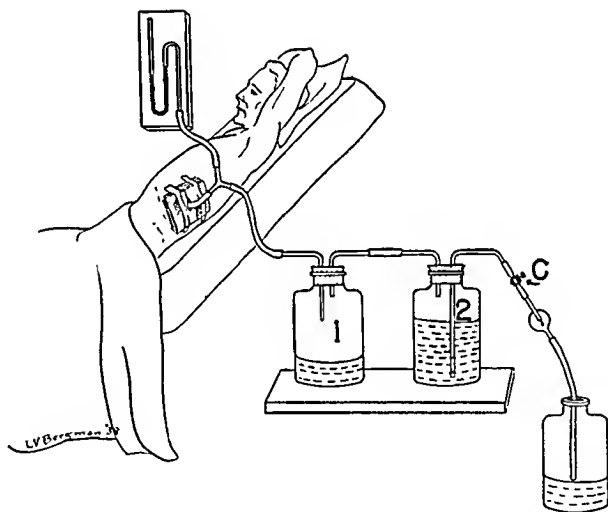


Fig. 2.

Fig. 1.—Shows the method of attaching the irrigating container and collecting bottle to the tube in the chest. The hemostat in position A prevents the fluid from entering the pleural cavity, but permits the pleural content to pass into the collecting bottle. When the hemostat is placed in position B, the irrigating fluid enters the pleural cavity.

Fig. 2.—Shows the attachment of the manometer and simple aspiration (siphonage) system. The stopecock at C is used to regulate the siphonage and negative tension.

the equilibrium of the system. In about a week or ten days the lung should be completely expanded. A roentgenographic examination of the chest should be made at this time. The indications for the removal of the tube from the chest are (1) an afebrile state, (2) complete expansion of the lung, and (3) a minimum of retained fluid. Occasionally, however, a small area of incompletely expanded lung may be seen in the region of the tube and/or a small amount of fluid below

the level of the tube. These are no contraindications to the removal of the tube. A strip of rubber tissue is then placed into the sinus to prevent too rapid healing of the wound and at the same time to permit drainage of any residual fluid. The opening in the chest wall is cleansed and a dry dressing is applied to it. This wound usually heals within a week or ten days.

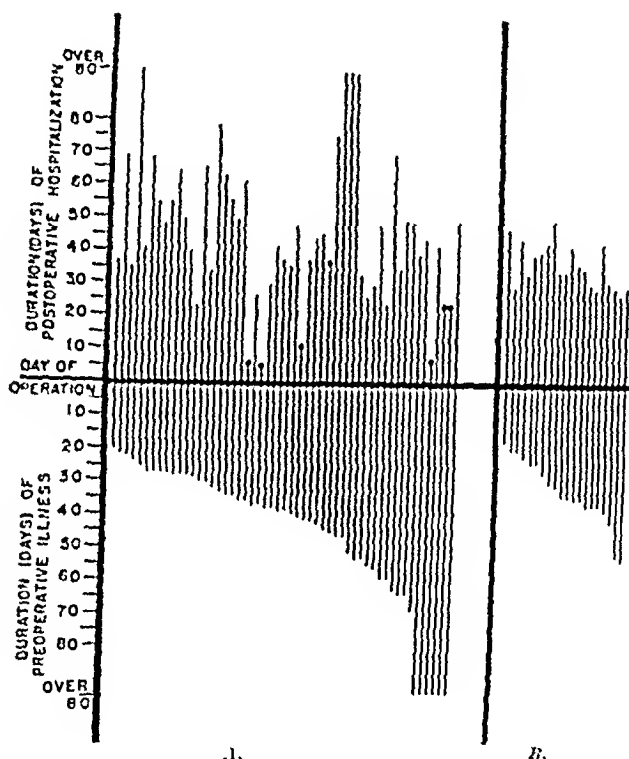


Fig. 3.—Shows the preoperative duration of the patients' illness and the post-operative period of hospitalization. Each vertical line denotes one case. This solid dot denotes a fatality and the postoperative day on which the patient succumbed. A denotes 53 unselected cases treated by methods other than negative tension. B denotes 20 unselected cases treated by irrigation and negative tension.

*Streptococcic empyema* is usually secondary to a streptococcic bronchopneumonia and occurs during the course of the latter disease. It is synpneumonia. The pus is relatively thin in the early course of the disease and is accompanied by a minimum of fibrinous coagulum. In the earliest stages of this disease repeated aspirations to relieve dyspnea, toxemia, or cardiac embarrassment may save the life of the patient. It is generally agreed that an empyema is not an emergent surgical condition. This is particularly true of the streptococcic empyemas. When the acute phase of the underlying disease has subsided, then the empyema may be considered as a surgical problem. The pus being thin and unaccompanied by fibrinous material, it is unnecessary, in most

cases, to evacuate the pleural contents through a large opening such as is obtained following rib resection. Secondly, the lung being non-adherent until rather late in the course of the disease the admission of air into the pleural space will increase the collapse of the lung and thereby increase the anoxemia. In streptococcic empyema a closed intercostal drainage will often suffice. The previously described slow subaqueous drainage, followed by irrigation and negative pressure aspiration, is applicable, as in the pneumococcic empyema cases. In the later stages of streptococcic empyema, i.e., those in which the pus has become thick, the procedure outlined for the pneumococcic empyemas may be followed.

We have compared the results of this method of treatment in 20 unselected cases of empyema with 53 unselected cases treated by rib resection or intercostal drainage without negative tension. The results are given in Table I. It will be noted that in those cases treated by irrigation and negative tension the postoperative period of hospitalization was 37.3 days; whereas, in the 53 cases treated by rib resection or intercostal drainage the time required was 47 days. In this latter group of cases there were 7 fatalities and therefore the average period of the postoperative hospitalization in the surviving 46 cases was 53 days. Examination of Fig. 2 shows that there were 39 cases treated by the usual methods in which the duration of the preoperative illness was the same as in the 20 cases treated by irrigation and negative tension. In this group of cases there were 4 fatalities. The postoperative period of hospital stay in the surviving 35 cases was 54 days. So that, regardless of how we compare the results, the morbidity is appreciably less in those cases treated by the method described.

#### COMMENT

No hard and fast rules can be formulated for any surgical procedure, especially in the treatment of empyema. All cases must be individualized; some will require longer subaqueous drainage (as the earlier streptococcic cases), others longer periods of irrigation (as in subacute or mixed empyemas), and still others will require longer periods of negative pressure aspiration (as in those instances in which there is thickening of the visceral pleura). In general, however, the above time is adequate for all cases. The one rule which may be considered as fixed is that whenever the patient becomes dyspneic or coughs a good deal or the negative pressure becomes too high, the tube just outside of the chest wall should be clamped for a few hours. At no time, however, have we had any such untoward symptoms. When they did occur, they were transitory and did not embarrass the patient's respiration.



TABLE I

A REVIEW OF 73 UNSELECTED SURGICAL CASES OF ACUTE (NONTUBERCULOUS) EMPYEMA, 20 OF WHICH WERE TREATED BY IRRIGATION AND NEGATIVE TENSION

Total number of cases	73
Number of cases treated by negative tension	20
Number of cases treated by other methods	53
Total number of deaths	7 (9.6%)
Total mortality in cases treated by negative tension	0 (0.0%)
Total mortality in cases treated by other methods	7 (13.2%)
Average number of post-operative days in hospital for the 73 cases	44.3
Average number of post-operative days in hospital for the 53 cases	47.0
Average number of postoperative days in hospital for the 53 cases minus the 7 fatal cases (46 cases)	53.0
Average number of postoperative days in hospital for the 20 cases treated by negative tension	37.3
Average number of postoperative days in the cases treated by other methods in which there was a similar length of pre-operative illness (39 cases), minus the 4 fatalities, or 35 cases	54.0

Finally, we may add that in the pneumococic cases the temperature usually drops to normal within the first three days after surgical intervention. In the streptococic cases it may take a day or two longer. The lung is usually completely expanded within ten days after surgical intervention. An x-ray examination of the chest should be made at this time before the tube is removed. If no contraindications exist, the tube may be removed.

At the present time we feel encouraged by our results of irrigation at the time of surgical intervention and the maintenance of postoperative negative tension in the treatment of the acute nontuberculous empyemas.

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## THE SPECIFIC GRAVITY OF THE PUS IN EMPYEMA

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WHEN should a thoracic empyema be drained? The answer to this question is important for it may influence the convalescence or even the life of the patient. That open operation done too early may be fatal was strikingly demonstrated in the postinfluenzal empyemas where the mortality dropped from 40 per cent to 4 per cent with delay in open drainage.<sup>7</sup> Graham and Bell<sup>4</sup> showed that many of these deaths were due to shifting of the mediastinum, diminished capacity of the contralateral lung, and asphyxia. If the patient survived this, a total pyopneumothorax often developed. Heuer,<sup>6</sup> Wangensteen,<sup>8</sup> Carlson,<sup>2</sup> Graham and Berek,<sup>5</sup> and in fact most authors in recent years have warned against premature open drainage in empyema. It has been generally accepted that time should be allowed for stabilization of the mediastinum and fixation of the lung before operation is performed. Conversely, undue delay is to be avoided for it permits thickening of the pleura and chronic empyema. Thus drainage at the optimum time will avoid fatal asphyxia, pyopneumothorax, or chronic empyema and promote rapid healing. The problem is to know what is the optimum time for drainage.

Most surgeons decide when to operate upon a patient with empyema by observing the course and duration of the disease and the character of the pus. They wait until the pus is "thick" or "creamy" or "will just pour" and infer from this that the process is localized to a walled-off abscess. This is ordinarily a safe method but since so much depends upon the change in the exudate it would appear desirable to judge it in a quantitative rather than a descriptive way. As pus thickens, the specific gravity should increase, so it was decided to measure this to see if it gave an estimate of the condition. Readings were obtained in 36 cases, of which 18 were due to the pneumococcus, 12 to the hemolytic streptococcus, 5 to *Staphylococcus aureus*, and 1 to the tubercle bacillus.

The cases of pneumococcus empyema showed a steady increase in the specific gravity of the pus during the first three weeks of the disease. The following readings were representative of average results: 7 days, specific gravity 1015; 9 days, specific gravity 1017; 14 days, specific gravity 1025; 15 days, specific gravity 1027; 18 days, specific gravity 1034; 21 days, specific gravity 1040.

It was noted that in about three weeks after onset the specific gravity of the pus reached 1040. It leveled off here and did not go higher no

matter how long the process existed. Some patients were operated upon without any difficulty before this level was reached. Whether or not this will always be true can only be determined by greater experience.

The pus in cases of *staphylococcus empyema* was much like that from the *pneumococcus* infections. In contrast to these the exudate in *Streptococcus haemolyticus* empyema had a lower specific gravity at a comparable time in the disease. Fig. 1 shows typical examples of this condition. Here it is seen that a slow steady elevation of the specific gravity occurs, with ultimate fixation at a constant level. When this stage is reached, open drainage of the chest should be a safe procedure.

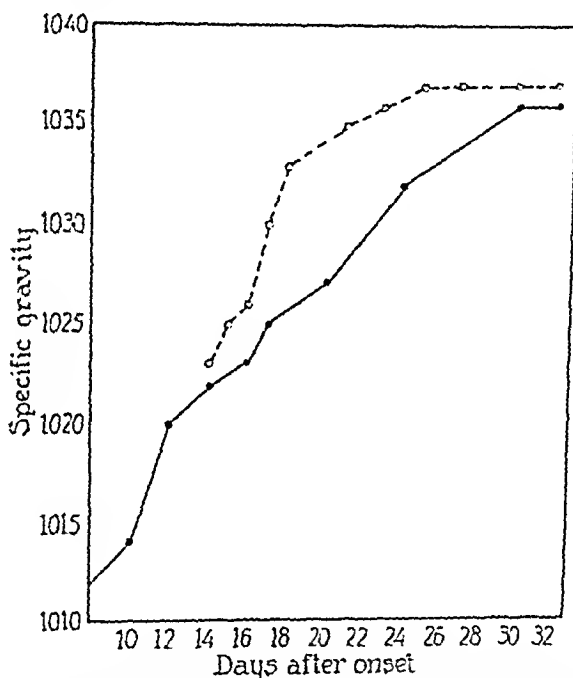


Fig. 1.—The rise in the specific gravity of the pus in two cases of *streptococcus empyema*. Note the tendency to establish a constant level at about four weeks after the onset of the disease.

#### DISCUSSION

Direct efforts have been made to determine a safe time for open drainage of empyema. Berman<sup>1</sup> observed cases under the fluoroscope and found that in normal individuals or in those with early empyema the mediastinum changed in width with respiration, being wide with expiration and narrow with inspiration. He stated that when the mediastinum ceased to move with respiration, then localization had occurred, so operation was safe. Yet apparently this only indicates fixation and stiffening of the mediastinum and does not show that the lung is attached to the chest wall. Until this attachment occurs, open operation may allow collapse of the lung with resultant pyopneumothorax.

Fraser<sup>3</sup> uses the level of intrathoracic pressure to determine the stage of an empyema. He states that the normal negative pressure becomes plus-minus with pleural effusion and positive with a localized abscess. The accumulation of pus in a walled-off infection creates a positive pressure. No mention of the use of this method was found in the literature, but it would appear to be valuable.

The study of the character of the pus is an indirect method of estimating the stage of the infection. It is simple and has been widely used. The measurement of the specific gravity of the exudate gives a quantitative expression to this estimate which makes for greater exactness. Other physical changes in the pus also may be indicative of the stage of the disease, so data are now being obtained on the viscosity, cell count, and hematocrit. Such information, if correlated with the clinical signs, should assist in an accurate estimation of the condition. It may tell us exactly when a thoracic empyema should be drained.

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# LYMPHOPATHIA VENEREA AND THE FREI TEST\*

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SINCE the advent of the Frei Test in 1925 as a specific means of diagnosing lymphopathia venerea, the literature has been flooded with articles concerning this disease. With the possible exception of carcinoma, there perhaps has been as much or more written on this subject in the last ten years as upon any other subject. Yet, despite such enthusiasm, there is an apparent feeling in some localities that lymphopathia venerea is still a rare disease. Or, on the other hand, there is a tendency to believe that it has become a "wastepaper basket" term, a name to be given to any lesion occurring about the genitals or rectum which presents no apparent etiology. That certain disease processes which are labeled lymphopathia venerea do exist is willingly admitted. But, there is an unwillingness to diagnose them as such, simply on the basis of the positive Frei test, although one may find some forty or fifty references in the literature favoring the specificity of this test.

Therefore, it was the purpose of this study to add further evidence as to just how specific the Frei test is, particularly in the study of certain genital and rectal conditions as seen in the colored race.

The patients studied were mainly those seen routinely in the Proctologic Outpatient Department of Baylor University Hospital, Dallas, Tex. All patients, irrespective of their complaints, were subjected to Frei tests. About sixteen different Frei antigens were used, with the thought in mind that patients might vary in their reactions, or that certain antigens might be more potent than others. The average variety of antigens given any one patient was 4.7; the most to any patient was 10. In many instances the patient was given repeated tests with the same antigen, it being felt that, in order to consider one as definitely having lymphopathia venerea, there should be a positive reaction either with most of the antigens used or a consistently positive response with the same antigen. Therefore, the greatest number of tests given any one patient was 15, the average per patient being 6.2. The total number of patients studied in this manner was 42.

Females	35
White	7
Colored	28
Males	7
White	0
Colored	7

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## CLASSIFICATION OF THE SYMPTOMS OF LYMPHOPATHIA VENEREA

Lymphopathia venerea is a disease with many syndromes. Usually the clinical manifestations can be placed in one of four general groups: inguinal adenitis, genitoanal involvement, rectal stricture, and urethral involvement. Of course, there will be more or less overlapping of groups, depending on the extent of the infection in any one patient.

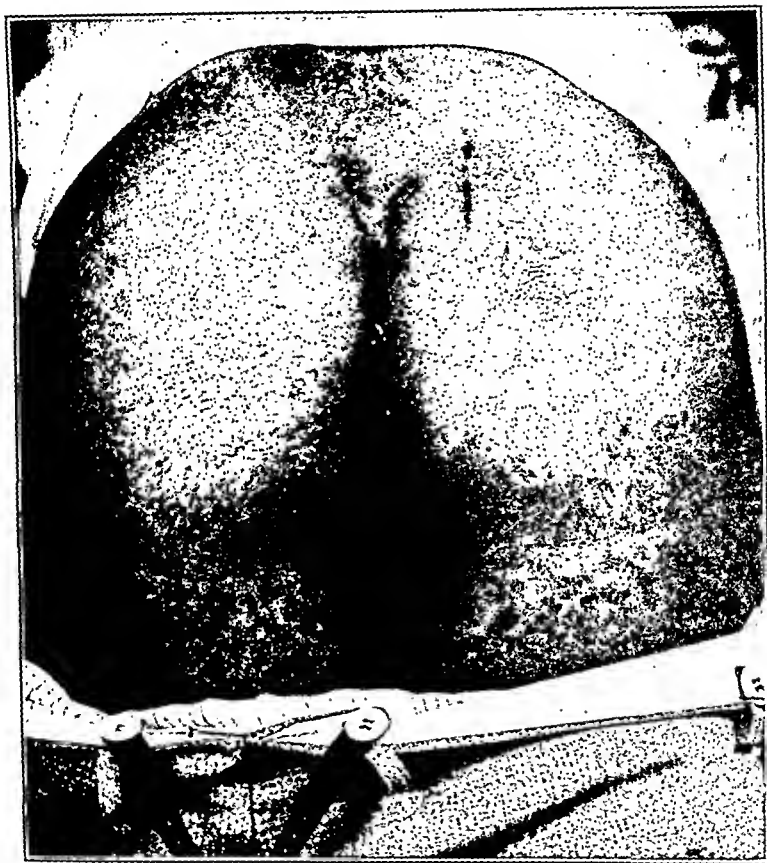


Fig. 1.—J. M., aged 32 years, colored male. There were some ten to twelve sinus tracts over the right buttock, which had been present for about six years. In addition, he had two more tracts opening upon the scrotum. No apparent connection with the rectum. Biopsy report: "Chronic inflammation of subcutaneous tissue with areas of focal necrosis. Etiology not apparent." Patient gave positive Frei reaction with three different antigens.

*Inguinal Adenitis.*—As has been so often described, this phase of lymphopathia venerea is seen most frequently in the male because of the difference of lymphatic drainage of the sexes. It is of interest to remember that as early as 1859 Chassaignac recognized this condition as a definite clinical entity, believed it to be of venereal origin, and gave a truly modern-day description of the involved lymph glands. It was, of course, Nicolas, Favre, and Durand, in 1913, who first be-

lieved the disease to be not only of venereal origin, but also an infection of the genital lymphatics as well.

Of the series of 42 cases studied, 5 were classed in this group (Table I).



Fig. 2.—Q. S., aged 25 years, colored female. The granulomatous mass pictured about the rectum and vagina had been present for about eight years. Had been surgically removed once, but returned. She complained of "bloody pus" coming from the rectum. Had consistently negative Wassermann, Kille, and Kahn tests, and denied ever having received antisyphilitic treatment. Gave consistently positive reactions to three different Frei antigens. See Fig. 3 for biopsy report.

*Genitoanal Syndrome.*—This group includes a great variety of pathologic processes seen in lymphopathia venerea, most often in the female. Elephantiasis of the vulvae and chronic ulceration of the labia, perineal body, and anal region were described by Hingier in 1848, and the name of "anorectal syphiloma" applied by Fournier in 1875. In addition to the elephantiasis and the esthiomene of the vulvae, there may be all sorts of fistulas and sinuses about the vagina, anus, rectum, serotum, and apparently even the buttocks (Fig. 1). Condyloma-like masses may occur about the vagina or rectum (Fig. 2). Many writers, in discussing rectal strictures, have described the presence of anal ulcers and fissures, anal fistulas, pruritus ani, hypertrophic anal tags, etc., as

a sort of prestenotic phase of stricture.<sup>1, 19, 31</sup> However, it would appear that many such conditions, particularly as seen in the negro, may be the result of infection with the virus of lymphopathia venerea and may be present without evidence of rectal stricture. Such opinion, however, depends upon acceptance of a positive Frei test in these cases as significant evidence of lymphopathia venerea.



Fig. 3.—Q. S. Biopsy report: "The section is cut in such a manner that the thickened epithelium with acanthosis shows cords extending through entire section. The spaces between these epithelial columns consist of loose, edematous fibrous tissue infiltrated with many plasma cells, a few eosinophiles, and lymphocytes. There are a few small areas of coagulation necrosis. The fibrous tissue is moderately vascular." Diagnosis: Infectious granuloma of the skin with marked hyperplasia of the epithelium.

Of the series of 42 cases studied, it was found that 20 might be placed in the so-called genitoanal syndrome group (Table II).  
*Rectal Stricture.*—There perhaps has been more written and more discussion about this phase of lymphopathia venerea than any other. It is of particular interest that, beginning with Copeland in the nine-



TABLE I

NAME	AGE	SEX	RACE	DURATION OF CONDITION	SEROLOGY
1. E. F.	24	F	C	1 mo.	negative
2. R. C.	21	F	C	1 mo.	positive
3. O. O.	20	M	C	1 mo.	negative
4. A. B.	23	M	C	1 mo.	positive
5. W. F.	49	M	C	2 mo.	negative

teenth century, when he believed rectal strictures were of venereal origin, the etiology of such has been blamed, almost chronologically, upon syphilis, tuberculous, and gonorrhea. Since the origin of the Frei test, practically all clinics are reporting rectal strictures as 100 per cent the result of lymphopathia venerea. It is now well known that most rectal strictures occur in the female and predominantly in the colored race. In this respect it should be remembered that in 1923 Rosser<sup>28</sup> brought forth the term "fibroplastic diathesis" as descriptive of the negro's tendency to form excessive fibrous tissue following infection or irritation. (Fig. 4.) It cannot be doubted that this factor alone is responsible for the appearance in our clinics of a higher percentage of colored than white women with rectal strictures of lymphopathia venerea origin. However, Mathewson,<sup>24</sup> in a report from San Francisco, brings forth a significant point when he finds that of 78 patients with rectal stricture, 60 were men.

Sixteen of the 42 cases in this series had rectal stricture (Table III).

TABLE II

NAME	AGE	SEX	RACE	CONDITION PRESENT	DURATION	SEROLOGY
1. J. M.	27	F	C	Anal ulcer	18 mo.	Positive
2. L. M.	20	F	C	Anal fissure	3 mo.	Positive
3. E. C.	26	F	C	Infected anal keloid	9 mo.	Negative
4. E. R.	19	F	C	Anal condylomas	12 mo.	Negative
5. Q. S.	25	F	C	Anal condylomas	8 yr.	Negative
6. A. G.	32	F	C	Anal fistula		
				Anal ulcer	3 yr.	Positive
7. F. W.	31	F	C	Anal fistula		
				Anal ulcer	3 yr.	Negative
8. L. E.	20	F	C	Anal fistula	3 mo.	Positive
9. D. J.	24	F	C	Anal sinus	1 yr.	
10. M. B.	25	F	C	Esthiomene	4 yr.	Negative
11. E. A.	55	F	C	Pruritus ani	20 yr.	Negative
12. L. R.	27	F	C	Granular proctitis		Negative
13. G. S.	28	F	C	Anal ulcer		
				Vaginal ulcers	1 yr.	Negative
14. A. R.	39	F	W	Urethral stricture		
				Anal condylomas		
				Hypertrophic anal papillae	2 yr.	Negative
15. L. S.	37	F	W	Pruritus ani	2 yr.	Negative
16. P. D.	39	F	W	Pruritus ani	1 mo.	Negative
17. C. L.	27	M	C	Scrotal fistula	3 yr.	Positive
18. R. B.	28	M	C	Scrotal fistula	1 yr.	Negative
19. L. B.	36	M	C	Anal fistula	5 yr.	Negative
20. J. M.	32	M	C	Buttock sinuses		
				Scrotal fistula	6 yr.	Negative

TABLE III

NAME	AGE	SEX	RACE	DURATION OF STRICTURE	SEROLOGY
1. M. W.	28	F	C	2 yr.	Negative
2. C. S.	76	F	C	9 yr.	Negative
3. J. B.	39	F	C	8 yr.	Negative
4. B. H.	26	F	C	4 yr.	Positive
5. H. P.	32	F	C	5 yr.	Negative
6. B. T.	23	F	C	7 yr.	Negative
7. E. L.	27	F	C	9 yr.	Positive
8. M. S.	44	F	C	2 yr.	Negative
9. C. J.		F	C		
10. G. W.	33	F	C	1 yr.	Negative
11. M. H.	27	F	C	5 yr.	Negative
12. A. J.	23	F	C	4 yr.	Negative
13. J. A.	27	F	C	2 yr.	Negative
14. I. Q.		F	W (Mex.)		
15. R. L.	28	F	W	1 yr.	Negative
16. N. M.	64	F	W	8 yr.	Negative

*Urethral Syndrome.*—Little seems to have been mentioned in the literature as to this phase of lymphopathia venerea as a specific entity. Yet, it would appear to be almost as important as a clinical manifestation of lymphopathia venerea in the colored male as the rectal stricture is in the colored female. Martin<sup>24</sup> estimates that 92 per cent of urethral strictures as seen in the colored male are the result of this disease. Here again, however, one wonders what part is played by the fibroplastic diathesis as described by Rosser, and the fibroplastic tendencies in negro urethral disease as indicated by Day as early as 1921. Gray,<sup>12</sup> in 1936, described 25 cases of urethral involvement in the female, of which 23 gave positive Frei reactions. As stated by him: "The disease presents a syndrome—a chronic urethritis, with or without intra urethral ulceration, which may remain extremely chronic and indolent or may proceed to urethral stricture, or to ulcerative destruction of the urethra; the ulceration may extend beneath the clitoris and labia, or about the introitus and deeply to the sides of the rectum; elephantiasis vulvae may be associated." In the series of cases studied in this clinic, there has been one such patient whose condition seems worthy of brief description.

A colored female, 42 years of age, presented the symptoms of pain and straining with defecation, evacuation of blood and pus from the rectum, and continuous dribbling of urine, all over a period of four or five years. Examination of her genito-rectal region revealed a chronic ulcerative process which had completely destroyed the urethra, the sphincter, and part of the trigone; there was a large opening between the vagina and rectum in the fore part of the vaginal vault; the rectum was stenosed and admitted only a small sound or rubber catheter. (Figs. 6 and 7.) Wassermann, Kline, and Kahn tests were negative. An x-ray of the chest showed chronically involved areas in the right chest, but repeated examinations of the sputum were negative. The patient gave positive tests with five different Frei antigens.

TABLE I

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				Anal ulcer	3 yr.	Positive
7. F. W.	31	F	C	Anal fistula		
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16. P. D.	39	F	W	Pruritus ani	1 mo.	Negative
17. C. L.	27	M	C	Serotal fistula	3 yr.	Positive
18. R. B.	28	M	C	Serotal fistula	1 yr.	Negative
19. L. B.	36	M	C	Anal fistula	5 yr.	Negative
20. J. M.	32	M	C	Buttock sinuses		
				Serotal fistula	6 yr.	Negative

days, for if a positive reaction still existed at that time, it could be taken as a definitely positive Frei test and not a reaction of a non-specific protein type. Likewise, it was found that those Frei tests which were to be positive would still be quite positive on the seventh day.

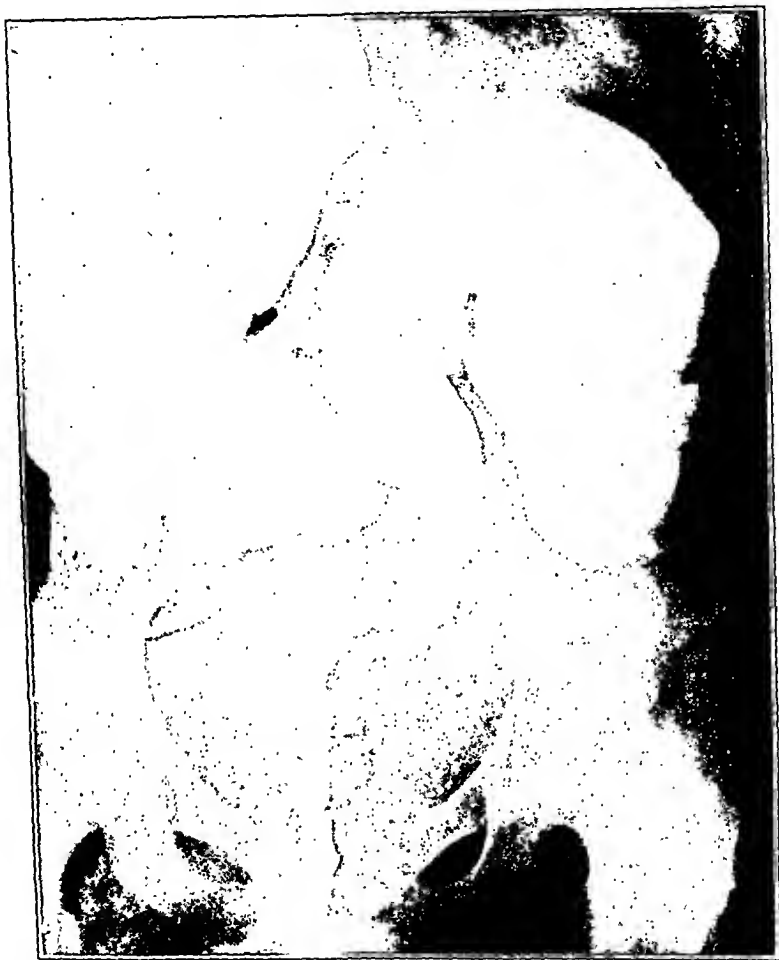


Fig. 5.—J. B., aged 39 years, colored female. Gave a history of rectal stricture of eight years' duration. Of interest in this x-ray, aside from the very evident stricture, are the numerous sinuses and fistulous tracts surrounding the rectal and sigmoidal canals. Serology negative. X-ray of chest negative. Gave very definite positive Frei reactions to seven different antigens. (See Fig. 8.)

About sixteen different antigens were used. These antigens were of a variety of sources, some having been made in the usual way from the pus of the involved bubo. Others were from macerated inguinal glands, or macerated tissues from fistulous tracts, perineum, etc. Some of the antigens were of a 1:5 dilution, others 1:10, and several 1:20. A few were of the polyvalent type, being a mixture of several different antigens from respective patients.

## THE FREI TEST

In this study the Frei tests were given in the classical manner, 0.1 c.c. of the antigen being injected intradermally. In most instances the reaction was not read until the end of seven days, although it is generally accepted that seventy-two to ninety-six hours is the optimum time to read such. There were two reasons for establishing the seventh



Fig. 4.—C. S., aged 76 years, colored female. Was known to have had a rectal stricture ten years ago, but it is not known how long it existed before that. About eight years ago had a colostomy because of the obstructive nature of the stricture. Six months ago it was necessary to repeat the colostomy as shown here, because of the excessive keloid formation which had choked out the previous opening as seen below the present colostomy. It is this excessive overproduction of fibrous tissue that Rosser calls "fibroplastic diathesis" and which must play an important role in the formation of rectal stricture in the colored race. This patient failed to react to Frei tests.

day as the time of reading. Most of the patients were, as has been previously stated, those in the out-patient department, and it was soon learned that the majority of them would return to the clinic rather faithfully once a week, but that about one-half of them would fail to make an appearance if asked to come more often. Also, it was felt that even more accurate readings could be made at the end of seven

upon them, or, who gave repeatedly positive tests with the same antigen and were checked against control patients, should be considered as having lymphopathia venerea as indicated by their Frei tests. The following summary, therefore, is based upon such considerations:

Inguinal adenopathy group	60 per cent positive
Genitoanal group	80 per cent positive
Rectal stricture group	81 per cent positive
Urethral syndrome (1 case)	100 per cent positive
Total for the entire group	78 per cent positive



Fig. 7.—X-ray of case pictured in Fig. 6. This shows the strictured condition of the anal and rectal canals. Note again, as in Fig. 5, the large sinuses and fistulous tracts leading off the rectal canal.

The second fact noted about the foregoing tables is that certain antigens gave more positive reactions than others. This would appear to be the result of either a variation in the patient's susceptibility to a

The positive reactions obtained were generally one of four types: a small papule, a large papule, a pustule, or an ulceration (Figs. 8 and 9). No effort was made to measure the size of the papule. If a definite palpable nodule was still present at the end of a week, the Frei test was considered positive.



Fig. 6.—L. C., aged 42 years, colored female. In this illustration the cavity seen just below the clitoris is the bladder and shows to what extent the urethra has been entirely destroyed. The whitish mass just below this is the anterior portion of the upper vaginal wall. The vaginal canal is not seen here, but the mere slit pictured just below the protruding upper vaginal wall is the entrance to such. The probe is seen to pass through a wide opening in the anterior vagina to the anal canal. There is much scarring and contraction about the anus with stenosis of the anal and rectal canals. (See Fig. 7.) Frei positive with five different antigens.

Tables IV-VII illustrate better than a verbal description the specific manner in which each patient responded to each Frei test. Each "x" is a positive test, and each "-" a negative one. The initials of each patient are plotted against the number of the antigen of the sixteen antigens used in the study. The patients in the various groups are listed identically with the previous charts.

From a study of these tables, two facts are at once obvious. In the first place, it will be noted that of the entire group of 42 patients only 2 or 3 failed to give a positive Frei reaction with at least one antigen. Therefore, because of the many and varied factors involved in a correct interpretation of Frei tests, it was felt that only those patients who responded positively to 50 per cent or more of the antigens used

upon them, or, who gave repeatedly positive tests with the same antigen and were checked against control patients, should be considered as having lymphopathia venerea as indicated by their Frei tests. The following summary, therefore, is based upon such considerations:

Inguinal adenopathy group	60 per cent positive
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The second fact noted about the foregoing tables is that certain antigens gave more positive reactions than others. This would appear to be the result of either a variation in the patient's susceptibility to a



given antigen, or a variation in the potency of different antigens. Coutts and Bianchi<sup>18</sup> have offered the explanation that such variations are due to subgroups of the virus responsible for lymphopathia venerea. Anderson and Harmos<sup>2</sup> found that antigens made from macerated inguinal glands were rather weak, and for the most part such has been

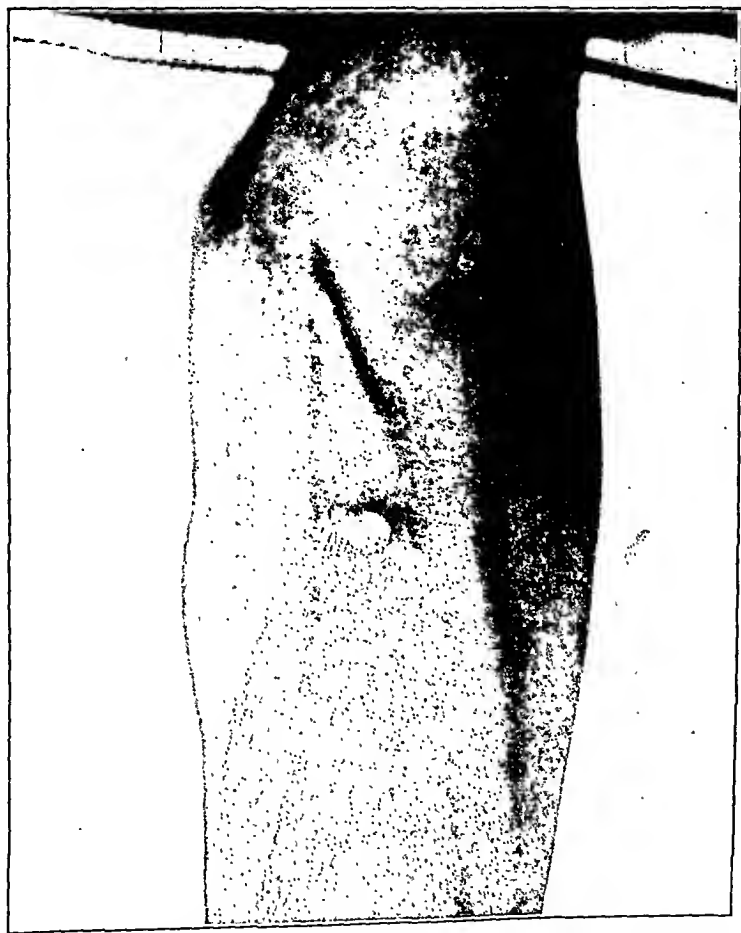


Fig. 8.—J. B. Same patient as shown in Fig. 5. Frei test as it appeared at the end of a week. She gave similar reactions to seven different antigens.

the experience of the author. Anderson and Harmos also report that the dilution of the antigen played very little part in the results obtained. Sullivan and Ecker<sup>33</sup> have stated that the present dosage of Frei antigen far exceeds the necessary amount. However, in this study there have been several patients who failed to give a positive Frei test, even with the more potent antigens, unless the dosage was increased. It has been said that the age of the antigen will vary the results obtained with it, that any antigen should not be used much

after six months from the time of its production. Several of the antigens used in this clinic have been three years old and yet have given good results. Such, of course, have been checked from time to time for evidence of bacterial contamination, and have been used upon other control patients.

Table VIII illustrates the variations of the antigens used in this clinic.

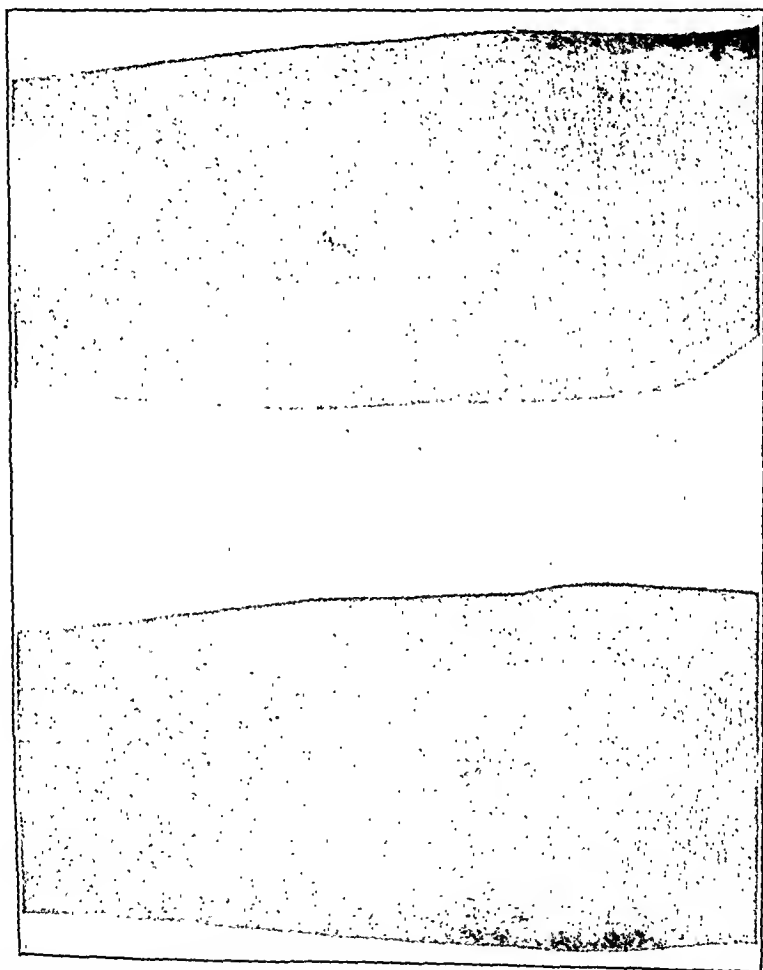


Fig. 9.—A. G., colored female with anal ulcer and fistula and history of purulent discharge from rectum for three years. This shows the pustular reaction and the ulceration as a result of two different Frei antigens given seven days before. A biopsy of the ulcerated lesion is shown in Fig. 13.

If we now consider the two previously mentioned factors, the variation in the patients and the variation of the antigens, and figure only those patients who reacted in a positive manner to 50 per cent or more of the antigens used upon them, and only those antigens which gave

TABLE IV

## I. INGUINAL ADENOPATHY GROUP

	A1	A2	A3	A5	A9	A10	A13	A14	A15	A16
1. E. F.	-	-	-X			-			XX	
2. R. C.			X	X				-		-
3. O. O.		XX	XX				-	-	-	-
4. A. B.					X					X
5.			XX							X

TABLE V

## II. GEXITOANAL SYNDROME GROUP

	A1	A2	A3	A4	A5	A6	A7	A9	A10	A11	A12	A13	A14	A15	A16
1. J. M.	X	XX	-X	X	X			-				-			X
2. L. M.	-	-	-	XX-X						-			-		
3. E. C.		XX	XX	XX	X	X	-						-		
4. E. R.	X	-					-								
5. Q. S.		XX	XXX	X	-			-	-				-		-
6. A. G.		X	XX		X	X		-	-		X	-	-		X
7. F. W.	-	XX	-	X		X		-	X-						
8. L. E.			XX		X										
9. D. J.					-										XX
10. M. B.			X												X
11. E. A.			X												
12. L. R.			XXX	X	X				X				X	-	XX
13. G. S.				X	X										XX
14. A. R.		-								X					
15. L. S.			XX	X	-										X
16. P. D.			-												X
17. C. L.	X	-X	-	-	-					XXX			-		-
18. R. B.		X	X												
19. L. B.		-	-	XX	-								-		X
20. J. M.		X	XXX		-			-	-			X	-	-	

TABLE VI

## III. RECTAL STRUCTURE GROUP

	A1	A2	A3	A4	A5	A6	A8	A9	A10	A11	A12	A13	A14	A15	A16
1. M. W.	XX	X	XX		X				-	X		-		-	X
2. C. S.	-	-X	X				-		-						
3. J. B.	X	X	X	X	X					-		-	X	-	X
4. B. H.	X	X			X	X				X		X			X
5. H. P.	-	XX	XX	X	X	-			X				-		
6. B. T.	X	XX	XX												
7. E. L.	X	X	X							-					
8. M. S.		-	-	X				-							
9. C. J.	-									-					
10. G. W.			XX			-				X					
11. M. H.		X	XX												
12. A. J.	-	XX	XX												
13. I. Q.										X					
14. J. A.		X						X			-				X
15. R. L.		X	X												
16. N. M.	X	XX	XX	X	X	X		X			-	XXX-			X

TABLE VII

## IV. URETHRAL SYNDROME

	A2	A3	A5	A13	A14	A16
1. L. C.	X	XX	-	X	X	X

TABLE VIII

ANTIGENS	AGE OF ANTIGENS	SOURCE	DILUTION OF ANTIGEN	NO. TIMES USED	POSITIVE TESTS	PER CENT POSITIVES
A1	3 yr.	B. pus*	1:10	18	10	55
A2	1 yr.	B. pus	1:10	41	30	73
A3	Fresh	B. pus	1:20	58	48	82
A4	1 yr.	B. pus		19	17	89
A5		B. pus	Poly #6†	20	12	60
A6	Fresh	B. pus	Poly #5	9	5	56
A7	1 yr.	B. pus	Poly #4	2	0	0
A8	6 mo.	B. pus	Poly #3	1	0	0
A9	3 yr.	B. pus	1:10	10	3	30
A10	3 yr.	B. pus	1:10	8	2	20
A11	1 yr.	B. pus	1:10	15	9	60
A12	2 yr.	Bubo		3	1	33
A13	Fresh	Fistula	1:10	12	6	50
A14	Fresh	B. pus	1:5	13	3	23
A15	2 yr.	Perineum		7	2	28
A16	Fresh	B. pus	1:5	24	20	87

\*B. pus, refers to inguinal bubo pus.

†Poly No. 6, etc., refers to antigens made from that number of different individuals, and is from bubo pus.

50 per cent or more positive tests of the total number given, we get the following results for the 42 patients studied:

Inguinal adenopathy group	80 per cent positive
Genitoanal group	80 per cent positive
Rectal stricture group	87 per cent positive
Urethral syndrome (1 case)	100 per cent positive
Total for entire group	83 per cent positive

#### PATHOLOGY

As with so many other phases of lymphopathia venerea, there has been much discussion in the literature as to the microscopic findings in this disease, and with no apparent unanimity of opinion. For the most part, whether the section be from an inguinal gland, a fistulous tract, or a rectal stricture, the microscopic appearance is one of sub-acute or chronic inflammation. Some have said there is a specific arrangement of epithelioid cells about the periphery of individual abscesses which are usually present. However, if sections are made of tissues from the genitoanal region of a patient with definite lymphopathia venerea and compared with similar sections made from a patient known not to have the disease, the microscopic appearance is very much the same (Figs. 10 and 11). A biopsy of a positive Frei test reveals only a nonspecific inflammatory process (Figs. 12 and 13).

#### DISCUSSION

If we are to consider the Frei test as a definitely specific means of diagnosing lymphopathia venerea, it then becomes evident that the

disease is much more prevalent than we had previously considered it to be, especially in the colored race. This is particularly true in that group of cases which present nothing more than anal fistulas, anal ulcers, pruritus ani, anal condylomas, etc. However, it is question-



Fig. 10.—Photomicrograph of section from anal fistula in colored female who was considered to have *lymphopathia venerea*.

able if the Frei test is sufficiently specific to be used as a routine method of diagnosis, unless one remembers and considers the various factors which alter, or may alter, the results obtained. Whether a Frei test will be positive or negative may depend upon any one of the following conditions: the presence of active syphilis; variations in the potency of different antigens; variations in the reaction of patients; presence of other diseases, such as chaneroid, active tuberculosis, and high fever;<sup>2</sup> and bacterial contamination of antigens. It

would seem, therefore, unwise to say that any condition suspected of being lymphopathia venerea is such, or is not, simply on the basis of one, or two, or even three Frei tests.

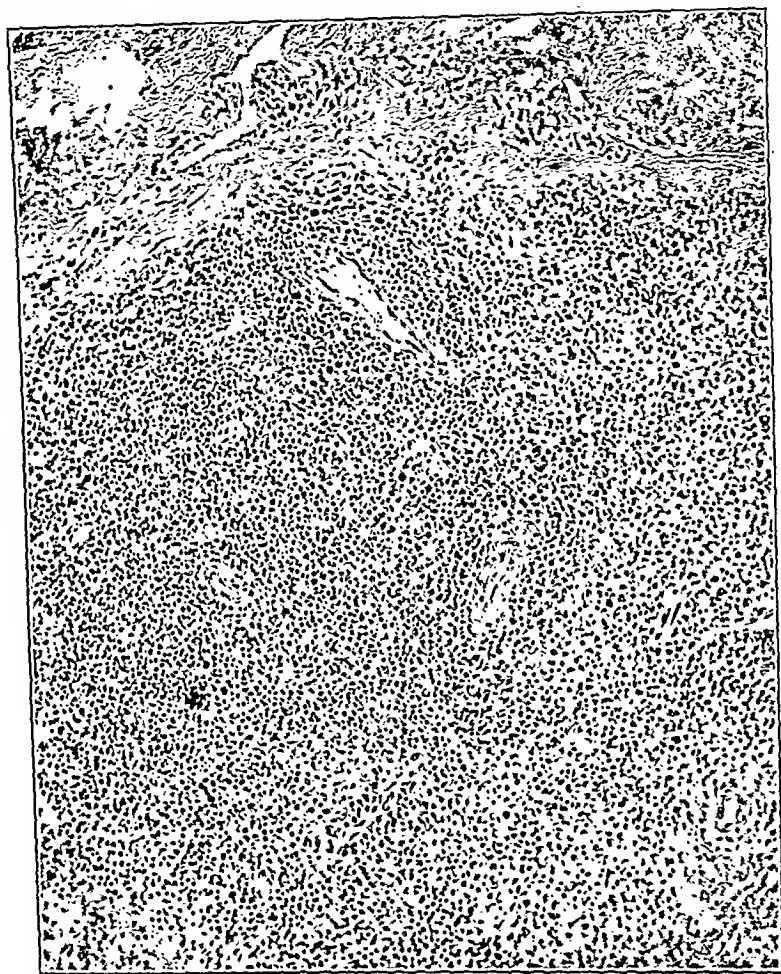


Fig. 11.—Photomicrograph of section from anal fistula in a white female not considered to have lymphopathia venerea. Note the similarity to Fig. 10.

#### CONCLUSIONS

1. The symptoms and clinical manifestations of lymphopathia venerea may be grouped into four major syndromes: inguinal adenopathy, genitoanal, rectal stricture, and urethral.
2. A single Frei test is not at all specific as a diagnosis of lymphopathia venerea.
3. If a number of different Frei antigens are used upon the same individual, the results may be considered as fairly accurate, and only then should the Frei test be considered as a specific test.

4. Lymphopathia venerea is apparently not a "wastepaper basket" term, for, of the 42 patients with genitorectal conditions studied, approximately 80 per cent were Frei positive.

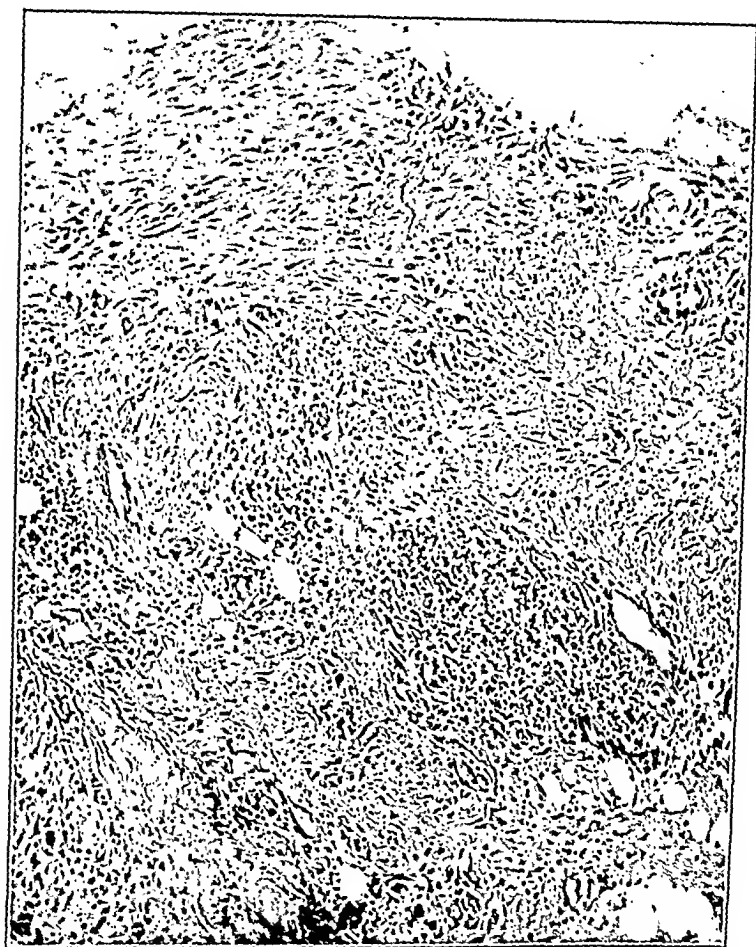


Fig. 12.—Photomicrograph of Frei test. As in Figs. 10 and 11, the main pathology is simply an infiltration of the subcutaneous tissue with numerous plasma cells, neutrophils, and a few eosinophiles.

5. On the other hand, it is questionable if all rectal strictures will be found the result of lymphopathia venerea if the Frei tests are carefully checked and rechecked. I refer particularly to those who would contend that 95 to 100 per cent of rectal strictures occurring in the colored female are due to this disease.

6. Also, it would appear that many of the cases of ordinary fistulas, ulcers, pruritis, etc., especially as occur in the colored race, are the result of lymphopathia venerea.

7. The microscopic pathology of lymphopathia venerea is that of a nonspecific inflammatory process.



FIG. 13.—Photomicrograph of positive Frei test. Of particular interest in this section, in addition to the cellular infiltration noted in the upper right corner, is the peculiar proliferation of stratified squamous epithelium in the lower portion of the section and which bears a fairly marked superficial resemblance to neoplasm.

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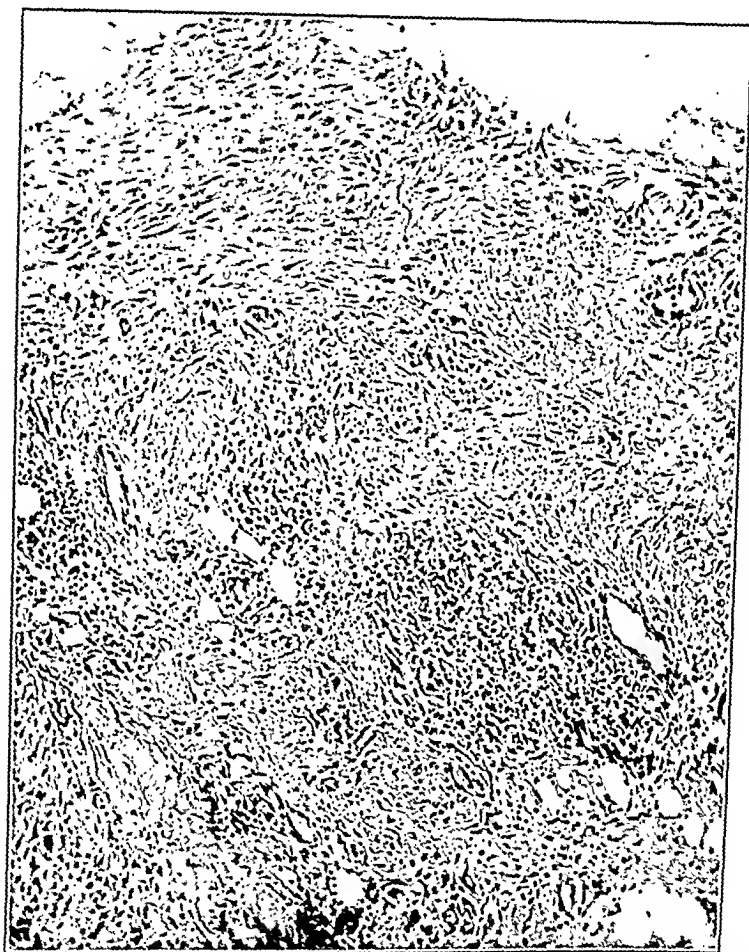


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# ELIMINATION OF PAIN FOLLOWING HEMORRHOIDECTOMY

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## INTRODUCTION

THE general practitioner and surgeon are confronted with few conditions causing more pain, suffering, and postoperative distress than are frequently encountered following hemorrhoidectomy. The laity are often so well "informed" that unnecessary postponement of both rectal examination and operation has naturally followed. To meet the demands of both patient and physician, there has been constant progress made toward rendering the postoperative phase of hemorrhoidectomy less painful and thereby making rectal surgery more acceptable to both patient and physician.

Oil-soluble anesthesia, originally introduced for the treatment of pruritus ani by Yeomans and co-workers<sup>6</sup> gradually has assumed a definite place in the alleviation of pain associated with anorectal surgery. Many oil-soluble anesthetics are now available and a few remarks will be made regarding them.

## OIL-SOLUBLE ANESTHESIA

The introduction of benacol by Yeomans<sup>6</sup> was soon followed by others, notably Gabriel's solution, mupercain in oil;<sup>1</sup> anueain introduced by Gorsch;<sup>2, 3</sup> proctocain, by Morgan;<sup>5</sup> and others.<sup>4</sup> Today there are probably a dozen or more oil-soluble anesthetics on the market and it seems desirable to point out that their indiscriminate use and their toxicity due to improperly selected drugs and unbalanced formulas have led to some undesirable results and adverse criticism. Oil-soluble anesthetics dispensed in ampoules and proved of clinical merit by more than one investigator should be selected. The decomposition products of the oils and alcohols, especially those contained in rubber-stoppered or unsealed bottles, will jeopardize the results of the most meticulous technician.

## SELECTION OF ANESTHETIC

A preparation should meet the following requirements: (1) It should be nontoxic. (2) It should produce both immediate and prolonged anesthesia. (3) There should be no delay in healing due to its use. (4) The cost of the solution should not prohibit its use in all classes of patients. If the solution itself meets the above requirements, then its more general use will rest upon the proper selection of cases and the proper technique of injection.

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cubic centimeters of solution is the usual amount used. It is felt that a  $2\frac{1}{2}$ -inch, 22 gauge needle fitted to a 10 c.c. Luer-Lok syringe with ring handles facilitates a smooth even distribution of the solution. The needle is inserted through the skin in the posterior midline approximately 1 inch distal to the anal margin. The injection is to be given, bilaterally, through two sites of os puncture, one each in the posterior and anterior midline (Fig. 1). Two well defined areas of distribution are used, a superficial and a deep (Fig. 2). No oil-soluble anesthetic should be injected intradermally, as slough will follow.

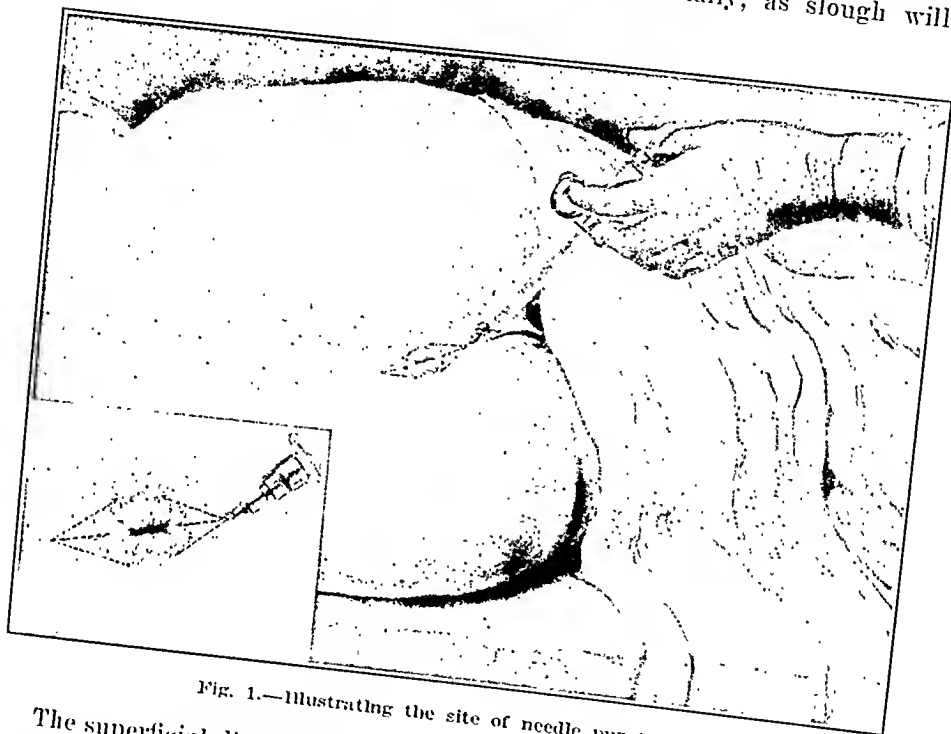


Fig. 1.—Illustrating the site of needle puncture.

The superficial distribution of the oil through the posterior insertion is a perianal infiltration of the subcutaneous tissues around the posterior three-fourths of the anus. About 2 c.c. of solution is thus superficially injected, particular attention being made to place some of it along the lateral margins of the subcutaneous external sphincter muscle. To prevent penetration of the rectal mucosa and to facilitate injection, the index finger is now inserted into the anus and through the same posterior site of injection the needle is guided so as to distribute the solution about the external and lateral margins of the entire sphincter muscles. Insertion of the needle into the tissues for  $\frac{1}{2}$  to  $\frac{3}{4}$  inch posteriorly and for  $\frac{3}{4}$  to  $1\frac{1}{2}$  inches posterolaterally along the sides of the muscle ordinarily will reach the principal innervation of this area which is from the inferior hemorrhoidal nerves.

## SELECTION OF CASES

In this particular report oil-soluble anesthesia was used in hemorrhoidectomies only. However, this type of anesthesia can be used in fissures, erythrit and papillitis, pruritus ani, external thrombotic hemorrhoids and a single uncomplicated combined hemorrhoid amenable to ambulatory operative treatment in selected cases, coccygodynia, and sphincter spasm as will be noted in the numerous references.

In this paper, if we consider the indications for injection to be elimination of pain following hemorrhoidectomy, the purpose has been served.

The object of injecting an oil-soluble anesthetic about the anus and rectum is manyfold. The production of prolonged and profound anesthesia about the anorectum is followed by prolonged relaxation of the sphincter muscles. This is accompanied by a remarkable freedom from postoperative pain and discomfort. If this can be accomplished without interfering with the healing of tissue and without the formation of induration, abscess, fistula, or deformity, we have a distinctly useful procedure in the realm of rectal surgery.

## CONTRAINDICATIONS

The important contraindications to injection are hemorrhoids accompanied by active suppuration in the form of abscess, sinus, fistula, and perirectal cellulitis, particularly that encountered in lymphopathia venerea (lymphogranuloma inguinale) of the rectum and anus.

Aged individuals whose sphincter mechanism is somewhat lax and atonic usually dislike the prolonged anesthetic effect as they are partially incontinent for the duration of anesthesia. Diabetics and others whose tissues appear markedly devitalized should be injected with caution and it is advisable to use the weaker solutions in smaller amounts in these cases. Particularly has this been found true for the solutions containing phenol or benzyl alcohol, either alone or in combination. Although this is not shown in this particular series of cases, it is mentioned due to my experience with several hundred injections of oil-soluble anesthesia in other anorectal conditions in which a few complications due to strong solutions or unbalanced formulas were encountered.

## TECHNIQUE OF INJECTION

The technique of injection has been particularly well described by Morgan<sup>5</sup> and Gorsch,<sup>2,3</sup> but for the sake of completeness, the method used in this series will be described.

At the time of operation, following the administration of the general, spinal, caudal, or trans-sacral anesthetic and before any operative procedure is started, the oil-soluble anesthetic is injected. Ten

## REPORT OF CASES

The same routine preoperative medication with barbiturates and morphine was given in both series of cases. This preliminary preparation in the experience of many has greatly facilitated the administration of a spinal anesthetic.

All patients were given a spinal anesthetic consisting of 90 to 100 mg. of novocain crystals dissolved in spinal fluid.

The Hirschman technique of ligature and excision of the pile mass was used in all patients. A radical hemorrhoidectomy was thus carried out. Clamp and cautery technique was not used in any case. The operative wounds in both series were not closed by suture in any fashion, as the Hirschman technique of operation is an open-wound method that heals by granulation. Suture and closure of the wound is invariably accompanied by more postoperative tissue edema, pressure, stitch infection, and inadequate drainage than the open-wound method. Postoperative spasm of the sphincter muscle which grips the operative wound sufficiently to produce ischemia, delayed healing, and postoperative pain is avoided if one does not stitch any suture material into the muscle where it acts as an irritating foreign body. At the conclusion of the operation, a thin strip of gauze, whose diameter in the anal canal would not exceed that of a lead pencil (often less), was inserted as a dressing in all cases.

The same routine postoperative care using warm compresses, Sitz baths, etc., was carried out in all cases.

The patients were out of bed and up on the second postoperative day, were given full diet from the second day on; had their first bowel movement usually the second day, and were given their first digital examination the third day. Patients on whom this radical type of hemorrhoidectomy was done are requested to stay in the hospital between five to eight days.

Table 1 shows the amount of narcotics used.

TABLE I

NO. OF DOSES OF NARCOTIC	0	1	2	3	4	5	6	7	TOTAL	AVERAGE
Series I										
Patients not injected	0	0	4	6	14	21	4	1	50 pt.	
Total narcotics	0	0	8	18	56	105	24	7	218 doses	4.02
Series II										
Patients injected	18	16	6	4	3	1	1	1	50 pt.	
Total narcotics	0	16	12	12	12	5	6	7	70 doses	1.4
Series II										
Corrected dosage						50-18 = 32 cases				
						32 cases : 70 doses				2.18

## ANALYSIS OF CASES

The analysis of these two series of cases has considerable comparative value and presents some interesting findings in regard to: (1) the amount of narcotic required to control postoperative pain; (2) the

Accurate and careful anatomic distribution of the solution is both possible and essential to obtain good results. Approximately 6 c.c. of solution is infiltrated into the deeper tissues in this fashion. The remaining 2 c.c. of solution is infiltrated, both superficially and deep, about the anterior fourth of the anus through a single anterior puncture. The distribution of the solution here blocks off the anal fibers of the perineal nerve which innervates the anterior fourth of the anus.



Fig. 2.—Illustrating the superficial and deep planes of injection. The subcutaneous area with the vertical shading shows the plane of injection obtained by inserting the needle along the line marked 1. The deeper injections are given along the lines marked 2, 3, 4, and 5.

The simple technique of injection must be strictly adhered to in order to get good results and avoid complications. By using a small gauge needle and keeping it in motion we avoid "pooling" of the solution. Abscess, fistula, and induration are known to follow errors in technique, mainly due to pooling of the solution or perforation of the rectum. Intradermal injection of any of the known oil-soluble anesthetics is invariably followed by slough.

that none of these patients had an absolutely painless postoperative course. The absurdity of some writers who publish and tabulate records indicating "no pain after operation" is a rather poor tribute to the average physician's mentality or to the patient's fortitude. I personally made the examinations in this series and know all of these patients had pain during their first digital examination. One thing was definitely noted; that, in general, the severity of the pain was less and the subsidence of the pain was more rapid in the injected group, Series II. In Series I, not injected, the pain was severe, the sphincter spastic, and the aftermath prolonged.

In Series II, injected, the pain was less severe and in many exceptionally mild by comparison. The sphincter was relaxed in all and in about 30 per cent of the cases it was actually gaping and patulous for many seconds after digital examination.

5. *The Extent of Surgery Done.*—In Series I, not injected, the usual technique of operation was used. The pedicle was ligated and the hemorrhoid excised so as to include a generous portion of skin. Hemorrhoidectomy was done in three quadrants in most of the cases and in a very small number excision was carried out in four quadrants.

In Series II, injected, the usual technique of operation was used in the first few cases. As it became more evident that the prolonged muscular relaxation and anesthesia would permit of more thorough postoperative digital examinations, the amount of tissue removed became greater. I would estimate that 70 per cent of cases in Series II had more hemorrhoidal tissue removed than those in Series I. The operation became more radical and it is safe to say the results more satisfactory. The incidence of postoperative skin tags became almost nil, and a smooth anus "without a vein in sight" became the rule. Series II, injected, definitely had a more radical operation.

6. *The Complications Incident to Operation.*—In Series I, not injected, there were 2 postoperative complications. In 1, a small thrombus developed in an island of skin left between the areas of excision. Linear incision of the overlying skin and evacuation of the clot relieved this immediately. One patient developed a sensitive scar which required the injection of a local anesthetic and freeing of the scar about two months after operation. None had developed stricture or abscess and there were no postoperative hemorrhages.

In Series II, injected, there was 1 case of delayed healing accompanied by a marked perianal erythema and pruritic dermatitis medicamentosa due to an idiosyncrasy to the solution. This was confirmed by the patch test. Prolonged sensory anesthesia or muscular weakness should not be considered a complication of these injected cases. This is desirable and constitutes part of the valid reasons for using the solution. However, it should be mentioned that all of these patients were cautioned that when any urge or desire to stool appeared



need for catheterization; (3) the ease of first bowel action; (4) the diminution in pain incident to postoperative digital examination; (5) the extent of surgery done; (6) the complications incident to operation. These will be discussed in order.

1. *The Amount of Narcotic Required to Control Postoperative Pain.*—In Series I, not injected, a total of 218 doses of narcotic were required. The average dose per patient was 4.03. Examination of the chart reveals that the dose range in this group was from 3 to 6. There were no patients in this group who were able to be comfortable without at least one dose of narcotic. The largest number of patients were in the group requiring 4 and 5 doses of narcotic and some of these individuals had nausea and vomiting directly attributable to the morphine.

In Series II, injected, a total of 70 doses of narcotic were required. However, in this series 18 patients (or 30 per cent) did not require any narcotic at any time after operation. This leaves a total of 32 patients (or 64 per cent) of the injected group who required narcotic for the average dose of 2.18. The dose range in this group was from 1 to 4. The largest number of patients were in the groups requiring 1 to 4 doses of narcotic.

2. *The Need of Catheterization.*—In Series I, not injected, 2 patients required catheterization. In Series II, injected, no patient required catheterization.

3. *The Ease of First Bowel Action.*—The usual regime in both series was a rectal instillation of warm oil on the morning of the second postoperative day. While it is impossible to chart the relief of such an intangible subject as painful bowel movement, a vast difference was noted between the two series.

Series I, not injected, had a greater tendency to delay the time of bowel movement. There was rarely a spontaneous action in this group. All had pain at the time of bowel movement and in a large number of patients the pain was more severe and was slower in subsiding.

Series II, injected, had less tendency to delay evacuation. Many had a partial involuntary passage during the first 3 to 5 days, and there were a few whose sphincter paralysis persisted for 12 to 14 days. About 50 per cent of the patients had pain at the time of bowel movement, but the severity of the pain was less and the subsidence of the pain was more rapid than in the other series.

In about 25 per cent of the cases, I would estimate that the pain of first bowel movement would be as severe in this series as it was in the group who were not injected. However, the subsequent passages usually would be much easier. In the entire group, with few exceptions, these patients were more comfortable during the intervals between bowel actions.

4. *The Diminution in Pain Incident to Postoperative Examination.*—This was painful to all patients in both series. It should be understood

## MAJOR OPERATIONS IN ELDERLY PATIENTS

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THE surgical care of those in the autumn of life has become a problem of enlarging interest and importance during the last half century because of the ever increasing number of patients over 70 years of age who present themselves for diagnosis and treatment. It is surprising to think that eighty years ago only one-half of our population reached the age of 40 years, while in 1931, as Brooks points out, the average age of the white male was 59 years and the white female 62 years. In other words, life expectancy has been increased by 20 years during the past eight decades.

Of a population of 122,000,000 in 1931, 6.6 per cent were over 65 years of age, or twice the number living in 1850. With this rate of increase projected over a similar period of years, there will be seven times as many people over 65 years, or about 28,000,000. From another point of view, a brief survey of the vital statistics of the Metropolitan Life Insurance Company is of interest. This shows that out of a group of 1,000 children of 10 years of age, over one-half will reach the 60's, while more than one-third will survive 70. There will be 145 octogenarians, and 8 of these will live for 90 years or more.

Responsible in part for this striking shift of our population is, of course, the medical profession. It has, through a wider distribution of intelligent medical care, created a responsibility which, although it may be a privilege to enjoy, is notwithstanding an enormous obligation.

First among the American writers to express an interest in the health of the aged were Chaveat and Loomis, who, in 1881, published a book on *Diseases of Old Age*. Nasher followed their example in 1912, while Thewlis made his valuable contribution to the subject in 1919. During the past twenty years many interesting and instructive articles have appeared which show an increasing interest in this growing problem of the surgical care of the aged. As Morten points out, the urologists were, by dint of sheer necessity, the first to realize the ability of the aged to withstand surgery with a surprising degree of resistance and in the face of the gravest physiologic adversities. Gradually, experience has shown that old age is no longer the contraindication to surgery that it was at the beginning of the century, and more and more data are being accumulated to substantiate this fact. Lazarus reported a case of a woman 85 years of age upon whom he had operated successfully for a ruptured, gangrenous appendix; Horsley

they should hurry to the bathroom immediately. Particularly was this true during the first week and in a few cases as long as fourteen to eighteen days. All developed normal sensation and muscular function following absorption of the anesthesia.

Although I had a few cases of induration and abscess in other cases, such as fissure and single thrombotic hemorrhoid treated in office practice, there were no such cases in this series. Improper solutions and errors in technique accounted for the above mentioned cases. Except as mentioned, delayed healing did not occur.

#### SUMMARY

In reviewing the notes on the charts and my own observations on these two series of patients, it was perfectly evident that in Series II, injected, we had a group of patients enjoying postoperative comfort to a degree not approached heretofore. There were many ways in which the daily observation of these injected cases differed from the other series. Patients who are comfortable to the extent of sitting up in bed, reading the paper, and partaking of a full diet on the first or second postoperative day were encountered rather frequently. Nausea, vomiting, and other signs of morphinism were largely eliminated. There were a few whose threshold of pain was not influenced completely by the injection, as indicated by the 32 cases. There were some in this Series II, injected, upon whom the injection of the oil soluble anesthetic seemed to have little effect. This is to be expected in the future. Although this is a small series of cases to report, the author feels that a review of a larger series would yield essentially the same information. The records and observations on these cases have been made personally and have been carefully kept and analyzed.

#### CONCLUSIONS

The following conclusions seem evident:

1. Oil soluble anesthesia is a valuable and efficient supplementary form of anesthesia available for hemorrhoidectomy.
2. Patients given an injection of oil soluble anesthesia have a more comfortable postoperative period as measured by (1) the amount of narcotic used, (2) the need for catheterization, (3) the ease of first bowel action, (4) the diminution in pain incident to digital examination.
3. Oil soluble anesthesia, properly used, permits of a more radical removal of hemorrhoid tissue, is not attended by delayed healing, and is rarely accompanied by any untoward sequelae.

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## PREOPERATIVE PREPARATION

The period of preoperative preparation is, of course, variable, depending upon whether elective or emergency surgery is to be done. However, every effort must be made to capitalize on what few natural resources the patients have managed to retain. No trouble must be spared in attempting to rehabilitate these elderly people as thoroughly as possible, for attention to such details may mean the difference between success and failure. There is no single group of patients in which, as Guthrie suggests, optimism, cheerful encouragement, and subtle management are so absolutely essential. Regimentation and the domination of a relentless and impersonal routine, or the sudden changes to which old people cannot adjust themselves readily, may be the sole cause of miserable failure. The aged frequently have accustomed themselves to reign supreme, and to thwart their harmless whims creates unnecessary conflict. On the other hand, and even more difficult to contend with, are a certain few who seem overpowered with a sense of hopeless futility. A prelude of soft restraint and gradual readjustment to surroundings and routine is, in elective surgery, as important as a cheerful attending staff of doctors, nurses, and visitors; while comfort, and pleasant food and quarters add materially to the *joie de vie* which must be infused into the patients.

Careful oral hygiene not only will increase dietary efficiency, but may prevent a not infrequently fatal postoperative parotitis. A well-rounded, high caloric diet, adequately supplied with vitamins and easily assimilated carbohydrates, will replenish any possible deficiency and re-establish a depleted glycogen reserve. Hydration with from 3,000 to 4,000 c.c. of fluid with an accurate record of the output will determine the water balance. Ten per cent glucose intravenously is the most efficient mild diuretic which may be used to combat an inadequate urinary output with a rising blood urea. It is also a valuable cardiac nutrient as well as a liver protective, although, of course, intravenous therapy must be governed by cardiac efficiency and limited at the first suggestion of decompensation. The correction of anemia not only will relieve the heart of a notable burden produced by inadequate oxygenation, but will restore it to more nearly normal the physiologic processes of these old people which, at best, function only at minimum efficiency.

If there is a previous history of cardiac decompensation or if electrocardiography reveals evidence suggestive of myocardial damage which under the additional strain of surgery may lead to heart failure, the question of preoperative digitalization presents itself. Inadequate digitalization is of no therapeutic value, and complete digitalization should be instituted only in the face of impending failure or actual decompensation. In the presence of such a complication, surgery is to be deferred when possible; otherwise prompt digitalization is the

has successfully resected the stomach for cancer in five patients over 70 years of age; Mayo and Nettrour have reported an interesting series of major surgical procedures in patients over 70; Yeomans and Newton, of Australia, each have reviewed a series of 100 such cases; Brooks, of Nashville, Tenn., discussed a group of 287 surgical cases over 70 years of age treated at the University Hospital during the ten-year period following 1925; and Gordon-Taylor states that to his knowledge the oldest person to be successfully operated upon was a 106-year-old woman who had a strangulated femoral hernia.

It was Osler's opinion that a deficient circulatory system is the true measure of old age, and, as is so often observed, some persons 50 years of age seem older than others of 70. However, tradition has it that the allotted span of life is three score years and ten, therefore those beyond this arbitrary point shall be considered in the old age group. Many who attain this age are alert, intellectually active, and anxious to live. They seek the surgeon in the hope that something may be done for them and are in a more receptive frame of mind when surgery is indicated. There is less interference from superstition, prejudice, and fear. From the surgeon's standpoint, pre- and postoperative care, technique, and anesthesia combine to afford the patient a far better prognosis than in the days of the frock coat and carbolic acid spray. However, due credit must be given these people, for without a sturdiness of fiber they would never have reached the age of 70 years. The end result is a steady increase in the operability of patients in this group with a concomitant fall in surgical mortality.

To assume this responsibility with credit to the profession, a carefully coordinated series of meticulously arranged details must be carried out with a precision and deftness that can be acquired only through a well-rounded surgical training and seasoned experience. The nicety of surgical judgment as to when, what, and how much to do is the keynote to success in these patients. It is, however, a futile attack unless adequately flanked and supported by thoroughly capable pre- and postoperative care.

A prompt and accurate diagnosis, of course, is essential, but here the examination has just begun. A searching study of the most intimate details of the patient's physiologic state must be made for these patients suffer from the burden of time and scars of previous disease in addition to the illness for which they present themselves. It is therefore important to evaluate as carefully as possible their reserve not only in order to determine their surgical limitations, but also to anticipate and thereby forestall any complications which may develop during the postoperative course, for, as Crile has observed, these complications are best treated before they arise.

In our series of 44 cases subjected to 55 operations, gas-oxygen-ether was used in 26 cases; local anesthesia was chosen in 21, sacral anesthesia proved satisfactory in 3 posterior resections of the rectum and in 1 vaginal hysterectomy; while local anesthesia supplemented with gas was used 4 times. Postoperative pulmonary complications occurred in 7 cases. One patient, with an ileocolostomy, died seventeen days postoperatively with bronchopneumonia; the anesthetic had been gas-ether. A second death from bronchopneumonia occurred four days after a secondary closure for wound disruption, done under local anesthesia. A third patient, an appendectomy done under gas-ether, developed a small area of bronchopneumonia six days postoperatively, but recovered. A fourth patient had a closure of a colostomy and amputation of the penis for cancer, done under local anesthesia at one time, and developed a mild bronchopneumonia; while in a fifth patient a small area of bronchopneumonia appeared on the fourth postoperative day following removal of a ruptured appendix under local anesthesia supplemented with gas. The only case of atelectasis followed a hernioplasty, done under local anesthesia. A sixth case died of bronchopneumonia on the sixteenth postoperative day following exteriorization of an esophageal diverticulum, under local anesthesia. The one death from pulmonary embolism had no relation to anesthesia and therefore will not be discussed with this group. In other words, the instance of postanesthetic pulmonary complications following 55 operations was 12.7 per cent. Of these, 2 occurred in the series of 26 which were given gas-ether, an instance of 7.6 per cent; while 4 followed the use of infiltration anesthesia in a series of 25 cases, a percentage of 16.8. Four of the infiltration anesthetics were supplemented with gas, with but 1 postoperative complication, an incidence of 25 per cent. Although this is not a large series, it shows conclusively that a good anesthetist, a short operative time, and careful postoperative care will render the use of general anesthesia in old people as safe as any other anesthetic available.

#### SURGICAL OBSERVATIONS

From the standpoint of technical accomplishment, it is perhaps superfluous to repeat that judgment, speed, and gentleness compose the essential trinnvirate for surgical success in these old persons. Little need be said about gentleness and speed except to emphasize that both tend to avoid shock as well as minimize the depth and duration of anesthesia, all of which have an extremely important bearing on the postoperative course. With regard to judgment, so many factors are involved that it cannot well be discussed in detail. Briefly, however, it is a question of how much surgery these patients can stand. Frequently this brings up the point of whether it is wiser to perform a single- or multiple-stage operation. Cohen has noted that secondary operations in these

procedure of choice. Obviously, the earliest postoperative evidence of decompensation is an indication for digitalization. The usual preoperative measures, such as cleansing of the colon, or gastric lavage, in surgery of the large bowel, or stomach, are such routine measures that they hardly need be mentioned here.

Laplace and Nicolson have studied the effect of prolonged recumbency in 34 patients confined to bed for orthopedic treatment who were otherwise in good health. One-half of these patients died, but of these 17 in only 10 was death directly attributable to prolonged confinement. These authors show that the continued inactivity of old patients confined to bed leads to a circulatory retardation with peripheral stagnation which is closely analogous to shock and that "local anoxemia and consequent degeneration of tissues leads to toxemia and to permanent capillary damage which perpetuates the circulatory fault and ultimately results in death." These conclusions obviously favor as short a period of recumbency as possible, with active or passive muscular exercise. Whenever practical, preoperative patients should be encouraged to be up and around during their preparation for surgery, and postoperative patients are to be mobilized as soon as possible.

#### ANESTHESIA

The question of anesthesia in the aged is still a problem open to discussion, but upon one point there is unanimous agreement; the anesthetist must be a good one. With this as a major premise, we find cause for a great diversity of preference among different surgeons. Thompson and Habin, in their series of 1,200 urological patients over 70 years of age, used spinal anesthesia almost exclusively. Keynes is partial to nitrous oxide and oxygen alone or in combination with avertin in elderly people, but he emphasizes the value of infiltration anesthesia. Crile disapproves of avertin or ether, but favors local anesthesia and uses spinal anesthesia regardless of the patient's age whenever sufficient blood can be given preoperatively. In Newton's series of 100 cases of major surgery in patients over 70 years of age, general anesthesia was used except in an occasional case in which there were obvious indications for local anesthesia. Nitrous oxide or ethylene was his choice whenever possible.

TABLE I  
ANESTHETIC

TYPE	NO. OPERATIONS	PULMONARY COMPLICATIONS	PERCENTAGE
Gas-ether	26	2	7.6
Gas-local	4	1	25.0
Local	21	4	17.2
Sacral	4	0	0
Total	55	7	12.7

In our series of 44 cases subjected to 55 operations, gas-oxygen-ether was used in 26 cases; local anesthesia was chosen in 21, sacral anesthesia proved satisfactory in 3 posterior resections of the rectum and in 1 vaginal hysterectomy; while local anesthesia supplemented with gas was used 4 times. Postoperative pulmonary complications occurred in 7 cases. One patient, with an ileocolostomy, died seventeen days postoperatively with bronchopneumonia; the anesthetic had been gas-ether. A second death from bronchopneumonia occurred four days after a secondary closure for wound disruption, done under local anesthesia. A third patient, an appendectomy done under gas-ether, developed a small area of bronchopneumonia six days postoperatively, but recovered. A fourth patient had a closure of a colostomy and amputation of the penis for cancer, done under local anesthesia at one time, and developed a mild bronchopneumonia; while in a fifth patient a small area of bronchopneumonia appeared on the fourth postoperative day following removal of a ruptured appendix under local anesthesia supplemented with gas. The only case of atelectasis followed a hernioplasty, done under local anesthesia. A sixth case died of bronchopneumonia on the sixteenth postoperative day following exteriorization of an esophageal diverticulum, under local anesthesia. The one death from pulmonary embolism had no relation to anesthesia and therefore will not be discussed with this group. In other words, the instance of postanesthetic pulmonary complications following 55 operations was 12.7 per cent. Of these, 2 occurred in the series of 26 which were given gas-ether, an instance of 7.6 per cent; while 4 followed the use of infiltration anesthesia in a series of 25 cases, a percentage of 16.8. Four of the infiltration anesthetics were supplemented with gas, with but 1 postoperative complication, an incidence of 25 per cent. Although this is not a large series, it shows conclusively that a good anesthetist, a short operative time, and careful postoperative care will render the use of general anesthesia in old people as safe as any other anesthetic available.

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patients most often prove fatal and therefore he condemns the multiple-stage procedure. C. W. Mayo reported 4 cases of patients over 70 years of age who underwent multiple-stage operations with success. In this series, 7 patients were operated upon two or more times, without mortality. Naturally it is unwise and unjust to prolong the period of invalidism unnecessarily by subjecting a patient to a series of surgical procedures when the same end can be accomplished without undue danger at one operation. However, these findings would suggest that multiple-stage operations may well be carried out upon elderly patients and that in those of questionable surgical tolerance it is perhaps best to err on the side of conservatism. A period of from two to three weeks or longer may be necessary between stages. Every effort must be made at rehabilitation before subjecting the patients to further surgery, so not infrequently the interval is prolonged. It is seldom that one or two additional weeks, during which time the patient may be up and around or even leave the hospital, will not be of material benefit.

#### POSTOPERATIVE CARE

Bodily warmth must be maintained during the transfer from the operating room to the bed on the ward. Patients should be turned frequently and inhalations of carbon dioxide, after the method of Graham, should be routine procedure. Deep respiratory excursions tend to aerate the bases of the lungs, which in old people are frequently congested or partially atelectatic, and in this way help to prevent pulmonary complications, which, as Harvey has said, occur six times more frequently in patients over 65 years of age than in those in the prime of life. Morphine is best used sparingly due to its depressing effect on the respiratory center and the cough reflex. Atropine in conjunction with it tends to decrease bronchial secretions and thereby facilitates a more complete aeration of all parts of the lungs. Pain, restlessness, and apprehension must be controlled, but with minimum sedation. The barbiturates are often poorly tolerated by old people and their effect is at times accumulative. This may serve to mask the early signs of renal insufficiency. The matter of hydration has been sufficiently discussed.

Postoperative transfusions are of importance in replacing blood loss, but a most striking effect may be seen in those patients who have lost momentum and for no specific reason are slowly but steadily failing. Massage of the extremities as well as active and passive exercise help to stimulate peripheral circulation and should be started as soon as practicable, to be repeated at regular intervals. Whittaker reported the case of an octogenarian who, following a gastroenterostomy, was gotten out of bed and allowed food on the third postoperative day.

## CLINICAL SURVEY

In this series of 44 patients over 70 years of age who have undergone major surgical procedures, it was found that 29 patients were between 70 and 75 years of age, while 15 were from 75 to 82: Average age, 73.5 years; oldest patient, 82 years; patients 70 to 74 years old, 29; patients 75 to 80 years old, 12; patients above 80 years, 3. Only 3 patients had passed the age of 80 years, and of these the oldest was 82. The average age of the group was 73.5 years.

TABLE II  
TYPES OF SURGERY

Elective operations	48	Malignant disease	24
Emergency operations	7	Benign disease	20
Colon and rectum	16	Pelvic	2
Biliary tract	7	Breast	4
Hernia repair	5	Exploration	1
Upper gastrointestinal	4	Appendix	3
Miscellaneous	2		

There were only 7 emergency operations performed in this series, while 54.5 per cent of the cases suffered from malignant disease. There were 16 colon and rectal cases, of which 14 were referred for carcinoma. One patient was found to have a carcinoma of the right colon. There were 8 cases of carcinoma of the sigmoid, while 5 patients suffered from cancer of the rectum. One patient had a diverticulitis of the sigmoid and another a lipoma of the mesentery of the sigmoid.

In 5 cases of malignant disease of the large bowel nothing more than colostomy could be done. Colostomy with subsequent posterior resection was performed in 3 cases, while an obstructive resection with complementary cecostomy was done 3 times. Ileocolostomy and right colectomy were performed in 1 case, and exteriorization for cancer of the sigmoid was accomplished in 2 cases. This latter procedure was likewise used in 1 patient with a lipoma of the mesentery and another suffering from diverticulitis.

Of the 7 cases operated upon for disease of the biliary system, 2 patients explored were found to have inoperable carcinomas, 1 of them having a cancer of the gall bladder, while the other was found to have a carcinoma of the liver, thought to be primary. Four patients were operated upon for inflammatory disease of the gall bladder with stones, and another, suffering from a painless, progressive jaundice, recovered following a cholecystgastrostomy.

Of the 5 hernias, 1 of the 4 inguinal hernias was strangulated, while the fifth was a large incarcerated multilocular postoperative ventral hernia. Of the 2 pelvic cases, 1 patient had a large ovarian cyst,

which was removed without difficulty, while the other, having a complete prolapse of the uterus, underwent a vaginal hysterectomy, followed by an uneventful recovery.

Three radical amputations of the breast were performed for carcinoma and 1 simple mastectomy was done for a papillary cystadenoma. One patient subjected to laparotomy was found to have an abdominal carcinomatosis, the origin of which could not be determined. Of the 7 cases of appendicitis and upper gastrointestinal tract surgery, 3 suffered from acute appendicitis, 2 being extremely acute, while the third was ruptured with an early peritonitis. One patient had an uneventful recovery following a radical resection of the stomach for a pyloric carcinoma, while a second patient with a cancer of the stomach died of a cerebral accident on the eleventh day following a radical resection. Another suffered from a perforated gastric ulcer for which closure and a posterior gastroenterostomy were performed. Recovery in this case was marred only by a transitory urinary obstruction from a benign prostatic hypertrophy. The last of this group was a patient with an esophageal diverticulum who died on the thirteenth postoperative day of bronchopneumonia following exteriorization of the diverticulum. One patient suffering from a mixed tumor of the parotid gland was operated upon successfully, while a second patient (82) with a cancer situated just anterior to the right tonsillar fossa underwent ligation of the right external carotid artery without mishap.

#### COMPLICATIONS

Of the 44 patients operated upon, 17 developed one or more postoperative complications, an incidence of 38.6 per cent.

TABLE III  
POSTOPERATIVE COMPLICATIONS

Total cases	Incidence 38.6%	Total complications	23
Bronchopneumonia	6	Cystitis	2
Acute retention urine	3	Atelectasis	1
Wound infection	3	Parotitis	1
Wound bleeding	2	Fecal fistula	1
Intestinal obstruction	2	Apoplexy	1
	Pulmonary embolism	1	

The commonest of these complications was, of course, bronchopneumonia, which occurred in 6 patients and was responsible for 3 deaths. Acute urinary retention from benign prostatic hypertrophy occurred in 3 cases. Wound infection followed 3 operations, while wound bleeding of moderate severity occurred in 2 of the infected cases, due to erosion of a small vessel. Postoperative intestinal obstruction occurred in 2 cases and was responsible for 1 death. Cystitis, a not infrequent complication following colon surgery, was present in only

2 instances. Pulmonary embolism, cerebral apoplexy, atelectasis, parotitis, and fecal fistula were responsible in 1 instance each. Recovery was complete in all but 6 of these patients.

TABLE IV  
MORTALITY

Patients	44	Operations	55
Males	27	Females	17
	Deaths	6	
	Mortality by patient		13.6%
	Mortality by operation		10.9%

In this series 6 patients died, an actual mortality of 13.6 per cent; or mortality by operation of 10.9 per cent. This compares favorably with statistics on this age group reported by other observers.

TABLE V

AGE	SEX	DIAGNOSIS	OPERATION	CAUSE OF DEATH	POST-OPERATIVE DAY
72	M	Cancer of the rectum	Colostomy	Intestinal obstruction	12
78	F	Cancer right colon	Ileocolostomy and resection right colon	Bronchopneumonia	17
71	M	Cancer rectosigmoid	(1) Obstructive resection (2) Secondary closure for wound disruption	Bronchopneumonia	12 21
73	M	Cancer of the sigmoid	Colostomy	Pulmonary embolism	
71	M	Diverticulum of esophagus	Exteriorization	Bronchopneumonia	13
72	M	Cancer of the stomach	Gastric resection	Apoplexy	12

Our first death occurred on the twelfth postoperative day from an intestinal obstruction following a colostomy in a 72-year-old male operated upon for cancer of the rectum. The second occurred on the seventeenth postoperative day following an ileocolostomy and resection of the right colon for cancer in a 78-year-old white woman who developed a bronchopneumonia. The third death was also from a bronchopneumonia developing twelve days after a secondary closure of a wound disruption which followed an obstructive resection and colostomy for cancer of the sigmoid. The fourth occurred on the twenty-first day following a colostomy for cancer of the rectum. This patient died from a pulmonary embolism. The fifth patient, operated upon for an esophageal diverticulum, died on the thirteenth postoperative day from bronchopneumonia. The last death occurred on the twelfth day of an unusually smooth convalescence following a resection of two-thirds of the stomach for carcinoma. This patient suffered a cerebral accident and died immediately.

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Of the 24 cases of malignancy, 8, or one-third, were found to be inoperable. Palliative procedures only could be used to aid these people. Two remain alive, the other 6 having died, the average length of life after operation being 3.1 months. Five cases of malignancy died in the hospital. Of the remaining 11, 3 who underwent radical surgery have died of a recurrence five, twenty-one, and twenty-five months after operation. Two patients who were subjected to surgical extirpation died twenty-one and twenty-six months afterward of causes unrelated to their previous illnesses.

Six patients, or one-fourth of the original group suffering from malignant disease, have survived radical operations for an average of 25.8 months without evidence of recurrence, which is in contrast to an average postoperative period of 3.3 months in patients upon whom palliative surgery alone could be performed.

Of the 20 cases suffering from nonmalignant disease, 18 are now living and well; therefore, of the entire group operated upon during the past five years, the average length of life has been 21.1 months, ranging from 6 weeks to 5 years. Of the 24 patients now living and well, the average length of postoperative life has been 16.9 months.

#### SUMMARY

1. The life expectancy of our population has been increased greatly during the past eight decades. There were 8,052,000 people over 70 years of age in our country in 1931 and this number is steadily increasing.

2. Much evidence has accumulated to show that elderly people tolerate surgery surprisingly well. There is a progressive increase in operability with a concomitant decrease in mortality in this age group.

3. Careful preoperative regulation and preparation are of vital importance in the success of surgery in these people. A thorough preoperative study aids materially in the management of postoperative care.

4. Of 55 anesthetics, 28 were gas induction ether; the rest were infiltration anesthetics, supplemented in 3 instances with gas. The postoperative pulmonary complications after ether were 2 as opposed to 5 following infiltration. The secret of this success is due to an extremely good anesthetist.

5. Upon surgical judgment depends the matter of when, what, and how much to do. The question of single- or multiple-stage procedures presents itself and the time interval between stages is discussed.

6. Postoperative care must be as meticulous as the preoperative preparation in order to forestall complications whenever possible, but they must be treated promptly and vigorously when they do occur.

## FOLLOW-UP

In the group of 16 colon cases, 4 died in the hospital and, of the remaining 12, 3 were found on exploration to be inoperable; therefore, only a colostomy could be done as a palliative measure. One of these patients is living six months after operation, while the other 2 died at four and nine months respectively. Of the 3 cases in which colostomy and posterior resection were performed, 1 is living and well after one year, another dead of apoplexy twenty-one months postoperatively, while the third lived for two years, to die of a recurrence of the malignancy. Of the 3 patients who survived cecostomy and obstructive resection, all are living and well, 2 at four and twenty-three months respectively; while the third has passed the five-year postoperative mark. Of the 3 patients upon whom exteriorization was performed, 2 are living and well at nine and fourteen months, while 1 died of unknown cause three months postoperatively.

Of the 7 cases of biliary disease, 2 were found to have inoperable malignancies and both died within two months of operation. The remaining 5 were living and well at intervals ranging from nine months to five and one-half years. Of the 5 hernia cases, 4 patients are living and well from five months to four years postoperatively, while 1 patient died four years after operation of an unknown cause. In the group of 4 upper gastrointestinal cases, 2 patients were included in the hospital deaths; 1 patient operated upon for cancer of the pylorus died of a recurrence twenty-five months postoperatively; the patient operated upon for perforated gastric ulcer is living and well four months after operation.

The patient upon whom a vaginal hysterectomy was performed for a prolapsed uterus is living and well at three and one-half years, while the second patient operated upon for a large ovarian cyst is living and well at nine months. Two patients who underwent radical mastectomy for cancer of the breast have died, 1 five months postoperatively with a recurrence, while the second died of dysentery after twenty-six months; a third is living without recurrence at seventeen months, while the patient upon whom simple mastectomy was done for chronic cystic mastitis is well after sixteen months.

Two patients operated upon for acute appendicitis are living and well after six months to three years postoperatively, while the third died of heart disease three years after operation. One patient, who was found at exploration to have a widespread abdominal carcinomatosis, died within a month of operation.

Of the last 2 cases, 1 was operated upon for a mixed cell tumor of the parotid and is living with a recurrence after four years; while the patient in whom ligation of the external carotid artery was performed for cancer of the tonsillar fossa is living two months after operation.

## A REVIEW OF WOUND HEALING AND THE MECHANICS OF DEHISCENCE

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(From the Surgical Service of the Flower and Fifth Avenue Hospitals)

FOR the past several decades the subject of wound dehiscence has found its way into the surgical literature with increasing frequency. It is only too apparent, after reviewing the reports, that this influx is due not to an increase in the incidence, but rather to an alertness by surgeons to an existing hazard. The sad commentary on its present status is the fact that the literature continues to report its incidence relatively unchanged.

In the present article I make no claims for original research. The only justification for it is to review some of the previous literature on the subject, to publish a series of cases illustrating its occurrence, and to analyze both the literature and these case reports of wound dehiscence in an effort to arrive at a more tangible means of eliminating this postoperative complication.

*Incidence.*—One advantage of this report over several of its predecessors is its accuracy so far as the incidence of eventration is concerned. The time element in this series of cases is sufficiently short to permit a vivid recollection of the details, thereby repudiating the criticism given to several other authors that their records were only as infallible as the record room from which they were obtained.

During the one-and-one-half-year period beginning Jan. 1, 1937, and terminating July 1, 1938, there were 2,526 intraperitoneal operations performed at the Flower and Fifth Avenue Hospitals. During the same period, there were 13 cases with dehiscence of the wound post-operatively, an incidence of 0.51 per cent. If the 208 inguinal or femoral hernioplasties which were performed during that period are deducted from the total operative procedures, the incidence of wound dehiscence in this series is 0.56 per cent. In spite of the fact that Maes and co-workers<sup>1</sup> have reported a case of eventration following a direct inguinal hernioplasty, which is a comparative rarity encountered in the literature, it would seem that the deduction of hernioplasties provides a truer indication of the occurrence of wound dehiscence.

*Mortality.*—Maes and others<sup>1</sup> postulate that the most important factors in determining the mortality are the underlying disease process and the physical status of the patient, rather than the wound disruption per se. While this may be true in a considerable number of instances, nevertheless, it cannot be doubted that the occurrence of wound disruption



7. A clinical survey of 44 patients over 70 years of age who underwent 55 major surgical procedures is discussed, with reference to types of surgery, postoperative complications, mortality, and end results.

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dominal incisions. It cannot be construed, however, as indicative of any particular significance that the greatest number of cases occurred in rectus incisions, since this was by far the most frequently utilized type of incision in the 2,318 operations reviewed. The preponderance of upper abdominal dehiscence coincides with the findings of the majority of investigators,<sup>3, 5, 8, 9</sup> but the minority group, as exemplified in the review of a ten-year series at the Charity Hospital in New Orleans, is sufficiently in evidence to prevent any dogmatic statements in this regard.

TABLE II  
TYPE OF INCISION THROUGH WHICH DEHISCENCE OCCURRED

Right upper rectus	5 cases	} 69.1% upper abdominal
Right upper Battle	1 case	
Left upper rectus	1 case	
Upper transverse	1 case	
Upper midline	1 case	
Right lower rectus	2 cases	
Lower midline	2 cases	

It will also be noted that a wound dehiscence in our series of cases occurred following a transverse incision, which is contrary to the findings of several previous authors. Meleney and Howes<sup>4</sup> in their report advocated a greater utilization of the transverse incision because of its freedom from disruption. White<sup>10</sup> stated that in his series of cases disruption had not occurred after intermuscular, Pfannenstiel, costal, or transverse incisions.

In the present series of cases, the only common type of abdominal incision utilized in this hospital which was not complicated by a disruption was the McBurney incision. Colp<sup>11</sup> reasoned that the McBurney incision, on an anatomic basis, should afford protection against dehiscence. Grace<sup>5</sup> substantiated this reasoning in his review of a fifteen-year period on the First Surgical Division at Bellevue Hospital, during which interval there were no disruptions through McBurney incisions. It must not be concluded, however, that this type of incision is impregnable, since a fair-sized series of cases<sup>1</sup> have been reported in which almost 50 per cent of the wound dehiscences followed appendectomies, and in approximately one-third of these cases the McBurney incision was utilized.

*Occurrence.*—There is probably nothing more appalling to the surgeon following an abdominal laparotomy than to discover an abnormal amount of sanguineous drainage on the dressing after an interval of several days. This phenomenon is an almost constant precursor of wound dehiscence. The drainage in these cases imparts an almost characteristic hue to the dressing which Fraser<sup>12</sup> has aptly described as a "terra cotta" stain. This is not to be confused with the dark glairy appearance of the wound margins following a dehiscence and

tion quite frequently will transform a fair operative risk with a good prognosis into a seriously ill patient with a poor prognosis.

In the present series of cases there was only one death, or a mortality rate of 7.7 per cent, following wound dehiscence. It is only when we realize that this is an extremely low mortality rate that the full significance of the hazard which wound dehiscence offers to a successful postoperative convalescence becomes apparent. Jenkins<sup>2</sup> in his comprehensive review of the literature found a mortality of 35 per cent in 1,294 cases. Other authors have reported varying rates as follows: Glenn and Moore,<sup>3</sup> 45.4 per cent; Meleney and Howes,<sup>4</sup> 44 per cent; Grace,<sup>5</sup> 39 per cent; Bettman and Lichtenstein,<sup>6</sup> 37.5 per cent; and Koster and Kasman,<sup>7</sup> 17.5 per cent. When we reduce all of the available statistics concerning the incidence and mortality into ordinary figures, we find that approximately 1 patient in every 450 upon whom we perform an abdominal section dies following wound dehiscence.

*Sex.*—In the present series of cases there was a predominance of the lesions among males, since 9 (69 per cent) of the patients were of that sex. It would be imprudent to conclude on the basis of such a small series of cases that this represents a true incidence in each of the sexes. Jenkins<sup>2</sup> in his review of 1,294 cases also reported a masculine predominance, but to a lesser degree. He reported 57 per cent of the cases in males.

*Age Incidence.*—Wound eventration has been reported in every age group from infancy to old age. The youngest member in the present series was 22 years of age, while the oldest was 67 years of age. The distribution of cases in the various decades is depicted in Table I. It should not be considered unusual that the greatest number of cases are found in the third, fourth, and fifth decades of life, since it is on this age group that the greatest number of operative procedures are invoked.

TABLE I  
AGE INCIDENCE OF WOUND DEHISCENCE

20-30 years inclusive	2 cases
30-40 years inclusive	3 cases
40-50 years inclusive	3 cases
50-60 years inclusive	4 cases
60-70 years inclusive	1 case
	13 cases total

*Type of Incision.*—The type of incision and its location have been dwelt on by many authors in relation to their liability to or freedom from wound dehiscence. Table II illustrates the various types of incisions and their frequency of dehiscence in the present series of cases. It will be noted that 69 per cent of the cases occurred in upper ab-

dominal incisions. It cannot be construed, however, as indicative of any particular significance that the greatest number of cases occurred in rectus incisions, since this was by far the most frequently utilized type of incision in the 2,318 operations reviewed. The preponderance of upper abdominal dehiscence coincides with the findings of the majority of investigators,<sup>3, 5, 8, 9</sup> but the minority group, as exemplified in the review of a ten-year series at the Charity Hospital in New Orleans, is sufficiently in evidence to prevent any dogmatic statements in this regard.

TABLE II

TYPE OF INCISION THROUGH WHICH DEHISCENCE OCCURRED

Right upper rectus	5 cases	} 69.1% upper abdominal
Right upper Battle	1 case	
Left upper rectus	1 case	
Upper transverse	1 case	
Upper midline	1 case	
Right lower rectus	2 cases	
Lower midline	2 cases	

It will also be noted that a wound dehiscence in our series of cases occurred following a transverse incision, which is contrary to the findings of several previous authors. Meleney and Howes<sup>4</sup> in their report advocated a greater utilization of the transverse incision because of its freedom from disruption. White<sup>10</sup> stated that in his series of cases disruption had not occurred after intermuscular, Pfannenstiell, costal, or transverse incisions.

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is probably due to the reaction in the wound and peritoneum, with a consequent outpouring of serosanguineous exudate.

The presence of profuse drainage, however, is not the only criterion of impending dehiscence which must be heeded in order to anticipate trouble from this source. Lahey<sup>13</sup> cautions, and justly so, that all patients with late or persisting postoperative vomiting or any obstructive symptoms should have their operative wounds carefully examined by the surgeon for any evidences of disruption.

It is well to know what to look for in order to anticipate such dire consequences, but it is also extremely valuable to know at what stage in the postoperative convalescence they may occur. In the present series, ten (77 per cent) cases of dehiscences occurred between the fifth and eighth postoperative days inclusive. The earliest occurrence of this disaster in the group was on the fourth postoperative day, while the latest was on the twelfth postoperative day. These figures approximate very closely the usual time during which disruptions are reported. Jenkins,<sup>2</sup> in his statistical analysis of all the available literature, found that the average time of disruption was 8.3 days postoperatively.

*Wound Healing.*—Before proceeding farther with a discussion of wound dehiscence, it might be advisable to briefly review the process of healing in a normal uncomplicated wound.

The healing of a wound is far from being a simple, logical train of events. There are many features of the process which are poorly understood and which are highly debatable. In spite of the many theories which are advanced concerning the nature of the process, there are certain definite fundamental facts about which there is almost universal agreement. Since this paper is designed primarily to be a clinical rather than an academic discussion of the subject, an effort will be made to forego debatable issues as much as possible and to present the views which are most commonly accepted.

When an incision is made through a portion of tissue, the amount of trauma and devitalization sustained by its constituent cellular elements is directly dependent upon the precision of the operator and the manner in which the wound is inflicted. A coat of fibrin quickly forms on the incised tissue area. Whether we subscribe to the physico-chemical or the physiologic theory on the formation of fibrin is immaterial; the fact that the fibrin is the primary stage in the healing process still remains. If there has been a considerable amount of cellular destruction in the original lesion, the process of phagocytosis will predominate in the initial period, as evidenced by large numbers of leucocytes and mononuclear cells in the substance of the newly formed fibrin. It must not be construed, however, that all other processes are in abeyance. There is a concomitant production of endothelial cells which grow into the architectural framework of the fibrin

from the capillaries of the healthy tissues and give it a cellular structure. The endothelium proliferates to form a vascular tree for the new tissue and from these endothelial elements the cellular structure of the healing wound is derived.

Howes and co-workers<sup>14</sup> have demonstrated experimentally that there is a quiescent phase or "lag period" in the healing of a wound during which its tensile strength per se is zero. This period usually extends for from four to six days. Clark<sup>15</sup> found that this period was susceptible to dietary control and could be reduced by a high protein diet. Harvey and Howes,<sup>16</sup> however, contradict this statement. They maintain that a high protein diet, while responsible for an acceleration in the rate with which the wound heals, does not alter the duration of the initial "lag period." Following the lag period, the tensile strength of the wound rapidly increases until the maximum level is reached in from ten to fourteen days.<sup>14</sup>

A later stage in wound healing, known as the contraction phase, during which there is a compression of the vascularity and an increase in the connective tissue elements, is governed by a variable factor depending on the age of the wound and by a constant factor proportional to the original size. In this phase of a healing wound an increase in dietary protein causes no acceleration and the process proceeds over a period of many months.

Epidermization of a wound is dependent solely on the age of the wound when all other factors are constant. Diet also has no effect on this portion of wound healing.

From this cursory résumé we see that in normal wound healing there is a definite sequence or course which it follows. Probably the most significant aspect in the healing of any wound, so far as the clinical application of the physiologic mechanism is concerned, is the presence of a lag period with its concomitant negligible tensile strength. It is obvious that during this period the wound requires support to maintain coaptation of its margins. It has been for this purpose that suture materials have been a necessary part of the surgical armamentarium since the time of the earliest available records.

*Suture Material.*—It would appear profitable at this point to consider the various types of suture material available to the surgeon for the purpose of re-enforcing a wound during the period in which it is intrinsically weak. For purposes of discussion we may roughly divide them into two distinct groups: first, absorbable suture material; and second, nonabsorbable suture material.

When one speaks of absorbable suture material, one is referring to a type of material which, when placed in a wound, ultimately will disappear due to the properties of the body tissue in which it is imbedded. Catgut suture is the most common and widely used example of this type of material. It has been prepared in various graded sizes

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Jenkins<sup>2</sup> clinically arrived at the same conclusion when he found that his results were better upon using small sizes of hard, tanned gut.

Thus far we have been concerned with the reaction of catgut sutures which were imbedded in normal tissue. The reaction of catgut in infected tissue is entirely different. It is acknowledged that regardless of the type of catgut which is utilized for wound closure in the presence of infection, it disappears at an abnormally rapid rate. Howes and Harvey<sup>19</sup> state that in an infected wound the intensity of reaction is directly proportional to the degree of chronicization and the amount of catgut imbedded in the tissues. Thus, we see that even the most favorable type of catgut suture material quite frequently may be inadequate in the presence of infection.

Nonabsorbable suture materials present an entirely different array of problems. As their name implies, these suture materials are not resorbed by tissue activity and as a result retain their initial tensile strength after being imbedded in the tissues. Notable among this group of suture materials are silk, silkworm gut, steel alloy wire, silver wire, and several commercially prepared types of suture material. Each type of material has its advocates who voice a preference both for a particular suture and a technique with which it may be utilized.<sup>4, 10, 21-23</sup> There are in general two methods in which these materials may be used: first, closure by layers with the nonabsorbable material permanently located at the site of the closure; and second, closure by a technique whereby the removal of the material from the wound may be accomplished at the termination of the process of healing.

It is an acknowledged fact that, if an infected wound is sutured by layers with a nonabsorbable material which is destined to remain in situ, the results are consistently unsatisfactory. The suture material is a foreign body in the tissues and as such acts as a nidus for the inflammatory tissue reaction, until it is expelled from the wound. This has been frequently demonstrated in the case of silk suture, although any nonabsorbable suture will act in a similar manner. It is obvious that the only indication for the permanent deposition of nonabsorbable suture material in any wound is a case in which there is unquestionably no infection. Glenn and Moore<sup>3</sup> caution in regard to silk suture that even in clean cases there must be no catgut used in the closure lest the tissue reaction excited by the absorbable suture become localized around some of the nonabsorbable type and persist. The limitations of this type of closure are fixed by the type of case. There is always the hazard that should a secondary infection occur in the wound an unsatisfactory termination to the healing of the wound may be anticipated.

The second method of utilizing nonabsorbable suture material is more conservative in its scope and more adaptable to varying condi-



with initial tensile strengths varying in proportion to the density of the material. Tanning of the gut has been found to decrease its susceptibility to resorption in an uninfected wound, thereby maintaining more closely its initial tensile strength over a longer period of time. Various methods of tanning with a variety of agents have been devised for this purpose, but probably the one having the most universal acceptance in chromicization. Rhoads and his co-workers<sup>17</sup> advocate tanned iodized catgut on the basis of experimental work indicating an average daily decline in tensile strength of less than 50 per cent. of medium hard chromic catgut. This view is not held by several of the leading manufacturers of catgut suture material who have discontinued the production of iodized catgut because their research departments revealed such suture material to have a variable absorption rate of iodine as well as an increased perishability due to the destructive action of the iodine on the catgut.

Brewer,<sup>18</sup> in his research for the Council of Pharmacy and Chemistry for the American Medical Association, found that heat-sterilized catgut offered the most consistently bacteria-free suture material when compared with catgut sterilized by chemical methods.

In the present discussion I will avoid reference to ten-day, twenty-day, and forty-day tanned catgut, since it has been showed that at best these are only relative evaluations of the potential life of the suture material when imbedded in tissue under comparatively normal conditions. It will be found more practical to refer to catgut as either tanned or plain, with the understanding that the more highly tanned a portion of gut is the more resistant it will be to resorption. If we wish to formulate these facts more compactly, they may be grouped into two rules: first, the strength of a catgut suture imbedded in tissue varies inversely at a constant rate as a function of time; and second, this rate of variation is directly dependent upon the degree of tanning. These facts are graphically illustrated by the experimental work of Howes and Harvey.<sup>19</sup>

Kraissl<sup>20</sup> calls attention to certain intrinsic factors in the catgut which will increase the rapidity of its dissolution. Since practically all catgut is supplied in tubular ampoules, he has demonstrated that there is a tendency for the gut to fray at the point of bending in the tube. Occasionally foreign bodies incident to its production may be found in the catgut. He also cautions that, due to the necessary dehydration coincident with the production of boilable varieties of catgut, there is a compensatory absorption of fluid by these sutures when placed in tissue, thereby inciting a more vigorous reaction. He also notes that the larger sizes of tanned catgut may be incompletely chromicized due to lack of penetration in the process, consequently lessening their resistance to absorption as well as hastening their absorption due to a larger area on which tissue activity might take place.

of omentum is allowed to insinuate itself between the cut edges of peritoneum and act as an expansile wedge due to its subsequent strangulation and engorgement. Several other authors<sup>23, 26</sup> have subscribed to this explanation. In view of the fact that the peritoneum has little tensile strength and that the brunt of the burden for maintaining coaptation between the wound margins is borne by fascial structures, this explanation accounts for the disruption of only the peritoneal layer.

Von Graff<sup>27</sup> propounded the view that wound disruption is dependent upon obesity and diabetes, or at least disturbed carbohydrate metabolism. The relative infrequency with which obesity and diabetes as a group are attended by wound disruption would tend to make this hypothesis very insecure, if not entirely untenable.

The culpability of incomplete anesthetic relaxation was stressed by Heyd<sup>28</sup> as a contributory cause to wound dehiscence. The presentation, however, of a series of seventeen cases of disruption by Koster and Kasman<sup>7</sup> with an incidence of 0.22 per cent under the perfect relaxation afforded by spinal anesthesia seriously detracts from this position.

During the past several years, allergy has been indicted, notably by Babcock,<sup>21</sup> Kraissl,<sup>20</sup> and Hinton,<sup>29</sup> as a potent factor in the causation of dehiscence. They maintain that some individuals, particularly those who have had a previous operation and have an allergic diathesis, may develop a sensitivity to catgut, chromic gut, or chromic acid salts. This sensitivity initiates an unfavorable wound reaction culminating in disruption when these materials are utilized in the repair of an operative wound. This theory, however, fails to explain those occurrences, such as three in the present series of cases which were repaired with a nonabsorbable suture material and which disrupted. Another point which vitiates the potency of this factor in wound dehiscence is the experimental work by Frugoni,<sup>30</sup> in which he demonstrated that due to its intrinsic character, being composed of albumoses rather than albumens, catgut has a relatively weak or negligible antigenic potency, although his work does not establish this point conclusively.

Hypoproteinemia has been advanced by several authors<sup>31, 32</sup> as a contributory factor to wound dehiscence in a certain small percentage of cases. It has been shown that in the presence of a protein deficiency there is a retardation in the rate of wound healing together with an accentuated decline in the tensile strength of the catgut supporting the wound. This has been corroborated by both experimental and clinical research, but it is advanced merely as a contributory factor. The dehiscence in these cases results per se because the material coapting the imperfectly healed wound margins withdraws its support before the tensile strength of the wound is sufficient to maintain this function.

tions which may arise in a wound. Although there are several techniques which utilize removable nonabsorbable suture material for closure by layers, the usual method in which this type of closure is employed consists of the insertion of through-and-through sutures at some distance from the wound margins so as to pass through the depths of the wound. In this manner the wound is supported by suture material of unchanging tensile strength which may be removed after the tensile strength of the wound is sufficient to meet its own needs, thereby eliminating a focal reaction should the wound be infected.

*Tissue Strength.*—Besides the tensile strength of the material which is utilized in a wound closure, another important factor must be taken into consideration; namely, the holding power of the tissue in which the suture is placed. When sutures are inserted in a tissue under tension, they produce definite changes in the tissue which eventually may result in a weakening of the suture line. Gratz<sup>24</sup> has pointed out that such weakening will vary directly with the elasticity of the tissues in which the sutures are placed. Elasticity is defined as that property which causes a body to resist deformation and afterwards recover its original size and shape. He found that connective tissues in the human maintain their elasticity when subjected to a stress parallel to the direction of their fibers to a minimal tensile strength of 7,100 pounds per square inch. When the stress is not parallel to the direction of the fibers, however, the shear phenomenon takes place and the minimal tensile strength is decreased. Howes and Harvey<sup>25</sup> found that the initial holding power of a stitch diminished by 50 per cent in the first two days and then remained constant until after the fourth day, when the healing strength of the wound overshadowed the strength of the stitch. They also demonstrated that only in fascia and similarly condensed layers of connective tissue is the holding power of the stitch greater than the tensile strength of the finest catgut. From these facts it would appear obvious that the keystone of adequate wound closure is fascial approximation. The tension on fascial tissue must be distributed in such a manner as to remain well within the minimal limits of stress for the area of tissue involved. In other words, the potential stress to which the suture line may be subjected must be borne by a sufficient amount of fascial tissue at the time of the wound closure if the incision is to be expected to remain intact.

*Etiology.*—In view of the facts which have been enumerated concerning normal wound healing, suture materials, and the holding power of tissues, it would be well at this point to consider their relationship with the etiology of wound disruption, and, more particularly, with the disruption of abdominal wounds.

Freeman<sup>23</sup> advanced an explanation for wound disruption on the basis of an inadequate peritoneal closure. He postulated that a tag

undoubtedly will result in the greater utilization of smaller sizes of tanned catgut in a meticulous manner; i.e., interrupted sutures with small tissue bites, such as is advocated for the use of nonabsorbable suture material destined to remain in situ. The unvarying tensile strength of nonabsorbable suture in a wound closure, however, will be a necessary prerequisite if we are to contend successfully with the various factors, such as infection, allergy, and hypoproteinemia, which may vitiate the stability of an absorbable suture closure. Moreover, these nonabsorbable sutures, whether they be silkworm gut, silk, silver wire, or steel alloy wire, must be placed in such a manner as to maintain an adequate coaptation and holding power in the tissues should an abnormal strain be placed on the suture line due to increased intra-abdominal tension. The easiest and most practicable manner in which this can be accomplished is by through-and-through sutures placed sufficiently near each other so as to distribute their tension on the fascial structures evenly and through a wide area. It would appear, on the basis of the present evidences, that the ideal closure of abdominal wounds consists in careful tissue approximation by fine catgut sutures re-enforced by an adequate number of nonabsorbable retention sutures which have been placed through all the layers at an optimum distance from the wound margins to insure their holding power.

#### CONCLUSION

In the present article a series of 13 cases of wound dehiscence is reviewed. The more rational utilization of both absorbable and nonabsorbable suture materials is advocated in keeping with the known facts concerning wound healing, suture tensile strength, tissue-holding power, and the factors influencing wound dehiscence.

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Increased intra-abdominal pressure, incident to retching, coughing, straining, or distention, has been the most frequently indicted factor in the cause of wound dehiscence.<sup>8, 9, 33</sup> Although several authors<sup>1, 6</sup> attach little significance to this etiology, owing to its relative frequency in any series of postoperative cases, nevertheless, its consistent occurrence in this complication cannot be justly disregarded. In the present series of thirteen cases, twelve had either cough or distention of an appreciable nature prior to the occurrence of wound dehiscence. The error has been made once again of attributing to the increased intra-abdominal pressure the causation of the dehiscence rather than allotting to it the contributory role which it justly deserved.

The crux of the etiology of wound dehiscence lies in the definition of the purpose for which suture material is used in a wound. The function of suture material is to maintain tissue apposition until the process of wound healing has progressed to such a degree that the tensile strength of the wound is sufficient to render such artificial support unnecessary. The surgeon, when repairing such a wound, must take into consideration all the factors which may be functioning during the interim before the wound itself acquires sufficient tensile strength, and he must provide measures to compensate for them. The solution of this problem will be arrived at only when a definite technique of wound closure is utilized which can fulfill all of these requirements. Whether a case develops a wound infection, an increased intra-abdominal pressure, wound allergy, or a state of hypoproteinemia postoperatively, the initial closure should have been such as to meet any stress which these conditions might impose.

Prophylaxis.—The elimination of postoperative wound dehiscence is entirely within the jurisdiction of the operating surgeon. It is no longer an abstruse complication for the investigation of the research laboratory. The question of whether the incidence of this distressing complication will be ultimately abolished rests in the hands of the clinician. The first approach to the solution necessarily will be a better understanding of wound healing, suture materials, holding power of tissues, and the action of the various conditions which may arise postoperatively in the wound. The fact that Baldwin,<sup>34</sup> utilizing a definite technique in closure, has been able to report a series of 16,465 abdominal sections without dehiscence offers clinical proof that the abolition of wound dehiscence is not a mere surgical Utopia. Kennedy's<sup>35</sup> report of not a single dehiscence during a period of thirty-six years at the Joseph Price Hospital, where an equally adequate but dissimilar technique was utilized, serves as added emphasis.

Undoubtedly, catgut suture will continue to remain the predominant medium utilized in wound closure. The adequate perception of the physiologic mechanism in wound healing together with an understanding of the decline in tensile strength of absorbable suture material

# THE USE OF SULFANILAMIDE IN SURGERY OF THE COLON AND RECTUM

## PRELIMINARY REPORT

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THE importance of postoperative peritonitis, retroperitoneal phlegmon, and extensive wound infections in surgery of the large bowel is fully realized. Analysis of the causes of death in published statistics from this and other countries indicates that peritonitis heads the list. The advances in the surgery of the colon and rectum in recent years have been in two directions. First, it has become increasingly evident that graded multiple-stage procedures are more desirable from all standpoints. The consensus of opinion seems to be that this point of view admits of little argument. Second, attempts have been made to develop some method which would vaccinate the peritoneum against infection. There is no need of an extended discussion of this phase of the subject at this time. Suffice it to say that neither the mixed vaccine recommended by Barger and Rankin, amniotin, nor any of the other recommended substances has produced the peritoneal immunity hoped for by their various proponents. Only recently, Rankin voiced his disappointment with the results of an extensive experience with the mixed vaccine of streptococci and *B. coli*.

About a year ago this study, the results of which are briefly reported herewith, was undertaken in the hope of throwing some light on the problem of postoperative peritonitis.

The work has been conducted by one of us (G. P. S.) in the Department of Bacteriology under the direction of Dr. Gregory Schwartzman, to whom we are indebted for invaluable advice and suggestions. Briefly, the plan of procedure consisted of: (1) the taking of cultures at the time of operation from the retroperitoneal and pericolic tissues, especially in the vicinity of the carcinoma; (2) under aseptic precautions, the bowel wall was incised in the region of the growth and cultures were made from all layers; and finally (3) cultures were made from the mucosal surface of the neoplasm. Both aerobic and anaerobic preparations were made in each instance. A more detailed report of this study will be made by one of us (G. P. S.) in the near future.

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sidered to be of the influenzal type. The peritoneal cavity was perfectly clean, as was also the perineal wound. The colostomy had been functioning properly.

The analysis of wound healing in these cases is of considerable interest. In only one instance was there a major wound infection and it was expected in this particular case. This patient had an obstructive resection for a perforated carcinoma of the sigmoid with a perisigmoidal abscess, and gross soiling of the wound and adjacent peritoneum occurred during the manipulations incident to freeing of the bowel. *B. coli* was recovered from the wound. Yet, in spite of this serious accident, convalescence was remarkably smooth. Another case of obstructive resection of the sigmoid developed a small stitch abscess. A third patient developed a mild infection of the posterior wound following an abdominoperineal operation.

In two cases of abdominoperineal resection for carcinoma of the rectum, the rectum was accidentally opened during the perineal part of the operation and gross spilling occurred. Yet, no infection developed and convalescence was uninterrupted. Finally, one of our most recent cases is of considerable interest. This patient, a woman 54 years of age, had a carcinoma of the rectum with considerable fixation to the posterior vaginal wall. Because of this, a two-stage Lahey operation was decided upon. During the course of the second stage, an abscess between the tumor and the vaginal wall was entered into and gross soiling of the peritoneum occurred. The operation was continued and a new pelvic peritoneal diaphragm was reconstructed. Except for a temporary mental upset attributed to the spinal anesthesia, convalescence was not marred in the slightest by this accident. There was no infection of either the anterior or posterior wounds. *B. coli* was cultured at the time of operation.

We have been impressed with the smooth uncomplicated convalescence of these patients, in spite of the fact that there have been no changes in operative technique. On this service, the one-stage Miles operation is usually employed for carcinoma of the rectum. Occasionally a two-stage procedure is decided upon for one reason or another. For neoplasms involving the transverse and left half of the colon, obstructive resections usually are performed. For carcinoma of the cecum and ascending colon, resection in one or two stages is done, depending upon the age and general condition of the patient. We have been using the so-called open type of anastomosis routinely. The improvement in postoperative morbidity and mortality, therefore, cannot be ascribed to any change in choice of operation or operative technique.

Before routine preoperative administration of sulfanilamide was instituted, cultures were made in six cases according to the method above described. These included 4 abdominoperineal resections in one



This study, which was started in January, 1938, soon showed that the predominating organism was a hemolytic streptococcus, associated in most instances with *B. coli*. On the basis of these findings, one of us (J. H. G.) suggested the use of sulfanilamide preoperatively as a prophylactic measure. The routine preoperative administration of sulfanilamide in all cases of small and large bowel surgery was started in March, 1938. Since that time, in a group of 21 consecutive cases that have been subjected to operation and cultured according to the plan above described, there has not been one positive culture of *Streptococcus hemolyticus* in either the retroperitoneal tissues, the bowel wall, or the mucosal surface of the neoplasms. The organisms demonstrated in these 21 cases may be tabulated as shown in Table I.

TABLE I

<i>B. coli</i> alone	2 cases
<i>B. coli</i> , <i>B. welchii</i> , enterococcus	3 cases
<i>B. coli</i> , enterococcus	10 cases
<i>B. coli</i> , <i>B. subtilis</i> , enterococcus	3 cases
<i>B. coli</i> , <i>B. pyocyaneus</i> , enterococcus	1 case
<i>B. coli</i> , enterococcus, <i>Staphylococcus aureus</i>	1 case
No growth	1 case

These 21 cases included the conditions given in Table II.

TABLE II

1. Abdominoperineal resection for carcinoma of rectum and rectosigmoid in one stage	5 cases
2. Obstructive resection for carcinoma of transverse, splenic flexure, descending and sigmoid colon	7 cases
3. Carcinoma of cecum	1 case
4. Colectomy for ulcerative colitis	2 cases
5. Two-stage Lahey operation for carcinoma of rectum	3 cases
6. Subtotal colectomy for multiple polyposis with carcinoma of sigmoid	1 case
7. Fibrosarcoma of ileum	1 case
8. Obstructive resection for acute suppurative sigmoiditis	1 case

In this group of 21 cases there were 2 deaths. One patient who had an obstructive resection for carcinoma of the splenic flexure experienced an uneventful convalescence until the seventh day when he suddenly went into collapse and died within five minutes. The clinical picture suggested either a pulmonary embolism or a coronary artery occlusion. There was no post-mortem examination. The second patient had an abdominoperineal resection for carcinoma of the rectum in one stage. His postoperative course was uneventful until the fifth day when he developed pulmonary edema quite suddenly. The clinical picture suggested coronary artery disease. Death occurred within six hours and at autopsy there was found a fulminating tracheobronchitis and bronchopneumonia which the pathologist, Dr. Paul Klemperer, con-

# Editorial

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## Fascia in Surgery

**D**URING the last fifteen years there has been a marked increase in the use of fascia in surgical conditions of all sorts. This applies to both sheets and strips of fascia, and to both autogenous and preserved. Fascia strips have been used as suture material in various conditions, to replace tendons and ligaments, and to hold various organs in position, or to fix certain parts that have lost their normal function, either through paralysis or operative accidents. Sheets of fascia have been used to repair fascial defects in various places, to reinforce suture lines, to furnish fascial bands for various purposes, and to keep raw surfaces apart, as in arthroplasty.

Fascia strips have been used as suture material more often in hernias than in other conditions. Indeed, it was the work of Gallie and Le-Mesurier on their "living sutures," a little more than fifteen years ago, that brought the use of fascia strips into such prominence. The strips have been used in the repair of hernias of all kinds, inguinal, femoral, umbilical, and postoperative. Some surgeons have gone so far as to use them as a routine procedure, while others use them only in their most difficult cases. There is a pretty general consensus of opinion that better results are obtained in difficult hernias when fascia strips are used than when other suture materials are used. However, a few surgeons deny this, claiming that the important thing is a correct apposition of the parts and that the type of suture material is a less important matter. It seems to me that both are important.

Among other uses of fascia strips as suture material might be mentioned their use in fractures, such as fractures of the olecranon and of the patella. They have been used successfully also in suture of acromioclavicular separation. They have been used also to suture defects due to spina bifida, to suture muscles to tendons, and to repair joint capsules, especially in the operation for habitual dislocation of the shoulder.

Fascia strips have been used to replace parts, or to fix parts, as follows: To replace the crucial ligaments of the knee; to supply tendon defects; to suspend the vault of the vagina when the uterine and round ligaments have previously been removed; to fix the corner of the mouth in facial paralysis; in congenital ptosis of the upper eyelid; and in the operation for complete incontinence of feces, using double bands around the anus and through the gluteus maximus muscles on each side, thus establishing voluntary control.

Sheets of fascia have been used to close hernial defects, the edges of which cannot be approximated, often strips of fascia being used to

stage, one Lahey procedure, and one obstructive resection for carcinoma of the transverse colon. In 4 instances the cultures revealed hemolytic streptococcus in association with *B. coli*. One case showed *B. coli* and an anhemolytic streptococcus, and the sixth cultured *B. coli* alone. In this group of 6 patients there were 2 major abdominal wound infections and 1 posterior wound infection.

Our routine preoperative preparation includes, in addition to a low-residue diet, glucose, transfusions when necessary, etc., the administration of sulfanilamide by mouth for three days before operation in 15 gr. doses every four hours day and night. We attempt to keep the sulfanilamide blood concentration between 5 and 6. Daily blood counts are done. It is important to watch closely for evidences of sulfanilamide intoxication. Many of the patients have developed the peculiar cyanosis frequently seen following the administration of this drug. In most instances, use of the drug is continued postoperatively for two or three days. No untoward results have been noted to date.

In order to amplify further the bacteriologic investigation, the results of which we have briefly reported in this paper, a change in procedure has been instituted. At the present time, every patient with a carcinoma of the rectum or rectosigmoid is sigmoidoscoped following a cleansing enema and cultures are made from the surface of the tumor, before sulfanilamide therapy is instituted. The results of these cultures will be compared with those taken at the time of operation. It is hoped that additional light will be thrown on the subject by these investigations. This phase of the work will be reported in detail by one of us (G. P. S.).

We have indicated in this preliminary report our experiences with the routine preoperative administration of sulfanilamide in surgery of the colon and rectum. It seems, after a careful evaluation of the clinical course of this group of patients, that the postoperative phase has been singularly uncomplicated, the morbidity has been unusually slight, and peritonitis has been nonexistent. In this connection it is important to note that, in 21 consecutive cases, *Streptococcus hemolyticus* was not recovered in any of the cultures made. It is realized that the number of cases reported herewith is not sufficient to warrant definite conclusions. However, the impression gained is that the results obtained so far warrant a continuation and extension of this study.

technical details that should be stressed is the testing of the strength of fascia strips before they are used. If fascia is cut on a bias, it has no tensile strength and will pull in two. Fat and excess areolar tissue could be carefully cleaned off. The presence of areolar tissue tends to produce a flimsy type of union instead of the firm type which ensues when the fascia is opposed to fascia without an intervening layer of areolar tissue. If one end of the strip is smaller than the other, the small end should be put in the needle and the larger end left free for anchoring. Care should be taken also to see that the anchoring is made in firm tissue and that all areolar tissue is cleared off from the area to be sutured before the suturing is started. In putting a needle through a fascia strip in anchoring, in splicing, or in putting in lock stitches, care should be exercised to see that the needle pierces the strip exactly in the center, else there is danger of tearing the strip. The ends of the fascia strips should be tied off with silk, linen, or steel wire, and not with some absorbable material. This, of course, also applies to suturing the strip in the needle. It is absolutely essential that the fascia strips stay in place long enough to ensure firm healing. If absorbable material is used to tie off the ends of the strips or to suture them into the needle, this is very likely to give way in a few days, as considerable tension is put upon it. If one such transfixion ligature gives way, the whole fabric of the repair is loosened. Likewise, it is essential that the final end of the suture line be firmly anchored in some appropriate manner, either by splitting the strip and tying, or by suturing the end firmly into some fascial structure with a nonabsorbable suture material. Since nonabsorbable suture materials are used, as just described, they should be used throughout the operation, both for ligatures and for other sutures, as it has been shown definitely that catgut and nonabsorbable sutures should not be used in the same wound. Use either all of one or all of the other. Infection supervenes much more often when they are mixed.

Finally it has been pointed out by a number of authors that infection does not necessarily vitiate the results in cases where fascia is used. Naturally, one would not expect the result to be as good in infected cases and infection necessarily results in some failures. However, many infected cases get excellent results and in the presence of gross infections, it is remarkable how little of the fascia sloughs out. In most cases only small pieces of fascia, a few millimeters square, are lost. In one case in which a large piece of ox fascia was used to repair a post-operative hernial defect, in which the edges of the defect could not be approximated, eventually two or three pieces of ox fascia strip, each about an inch long, that had been used to suture in the sheet of fascia came out. However, the sheet remained in place, and the result was a cure of the hernia.

—Amos R. Koontz, M.D.  
Baltimore, Md.

suture in the sheets. They have also been used to strengthen suture lines after hernial defects have been repaired under some tension, or when the structures used in making the repair have been weak. Sheets also have been used to repair dural defects, in arthroplasties, and to make cylinders to bridge tendon defects. Bands of fascia have been used to replace annular ligaments, to hold fractures in apposition, and around the aorta in cases of aneurysm.

Both autogenous and preserved (ox fascia) fascia have been used in almost all the conditions mentioned above. In our experience, both experimental and clinical, one is found to work as well as the other.

The results reported from various parts of the country in the use of fascia, especially in its use for hernia repair, have been somewhat inconstant, both with regard to autogenous fascia and ox fascia, but more specially with regard to the latter. It is quite probable that in those cases in which poor results have been obtained, the fault has been due to technical errors of various sorts. For a time bad results were obtained when ox fascia were used, due to a manufacturer's error in putting the strips up in an irritating solution. That error has long ago been corrected, and the strips are now put up in 1 per cent biniodide of mercury in alcohol. This is necessary to insure sterilization, as the strips cannot be taken out of oxen in slaughter houses in an aseptic manner. However, before ox fascia strips are used, all of the preserving fluid should first be washed out carefully in salt solution, otherwise there will be some chemical irritation in the wound as a result. The strips should be washed thoroughly in one basin of salt solution and then rinsed in another. It is the practice of some surgeons to let them soak for a couple of hours before using them. The point of thoroughly washing the strips in salt solution before they are used, has been mentioned before, but I believe has not been sufficiently stressed. It is a very important point and upon it depends satisfactory results in the use of ox fascia strips. Once the strips are free of any trace of chemical, they are entirely nonirritating, and the collagen fibrils in them differ in no way from those of autogenous fascia. In either case, the collagen fibrils simply act as a framework for the ingrowth of fibroblasts and blood vessels from the tissues of the host, because in the case of autogenous fascia grafts the cells between the fibrils die and have to be replaced.

It is often stated that autogenous fascia plays an active part in repair while preserved fascia plays a passive part. That this is an erroneous view is obvious from what has just been said about the manner of "taking" of both implants. The mechanism is the same in the one as in the other.

In the use of fascia, as in the use of any other surgical procedure, attention to technical details is a matter of great importance. Fascia has no magical qualities and its use in a sloppy manner will give results just as poor as, or poorer than, if it had not been used at all. Among the

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the methods of treatment employed at the Hospital of the University of Pennsylvania in a series of 155 cases was reported by Ravdin and co-workers.<sup>66</sup> Both the need for a prognostic test and the need for effective methods of treatment have been met since by the discovery of the relation of vitamin K and prothrombin to the hemorrhagic tendency in obstructive jaundice.

#### PROTHROMBIN

In 1935 Quick<sup>57</sup> introduced a new method for determining prothrombin in plasma. He observed that the Howell<sup>43</sup> prothrombin method was relatively insensitive to dilution of the plasma specimen. The two most widely accepted theories of blood coagulation, that of Moravitz<sup>54</sup> and that of Howell,<sup>43</sup> agreed on four necessary constituents for clot formation: prothrombin, thromboplastin, calcium, and fibrinogen. The presence of an optimum amount of fibrinogen has been demonstrated to be constant except after total hepatectomy or in the terminal stages of liver injury.<sup>55, 51</sup> In the Howell method an optimum amount of calcium was added, but two variables, prothrombin and thromboplastin, remained. Quick<sup>57</sup> showed that by the addition of an excess of thromboplastin in the form of suitable tissue extracts the prothrombin time could be reduced to a fraction of the figure obtained by the older method. He developed a test for prothrombin suitable for the clinical laboratory which depended on the addition of a rabbit brain emulsion to oxalated plasma before recalcification.

Using this method Quick, Stanley-Brown, and Bancroft<sup>62</sup> were able to demonstrate a prothrombin deficiency in a number of jaundiced patients and stated that this deficiency was the cause of the hemorrhagic tendency. Quick has since modified the test several times but the principle has not been changed.<sup>58, 61\*</sup>

A test for coagulability similar to Quick's method for prothrombin has been employed by Schönheyder<sup>70</sup> and by Dam and Glavind<sup>25</sup> based on a method of Fischer.<sup>34</sup> According to this method, instead of determining the time of coagulation of the unknown plasma, one compares the concentration of the thromboplastin preparation required to clot

\*Attention is called to what the author believes are typographical errors in the descriptions of two of Quick's methods.

With the method described in the paper entitled "A Study of the Coagulation Defect in Hemophilia and in Jaundice" by Quick, Stanley-Brown, and Bancroft in the *American Journal of the Medical Sciences* 190: 501, 1935, more satisfactory results have been obtained if 0.2 gm. of the dried rabbit brain is emulsified in 3 c.c. of physiologic saline solution instead of 0.3 c.c.; and in the paper entitled "The Nature of the Bleeding in Jaundice"<sup>61</sup> more satisfactory results have been obtained if fortieth molar calcium chloride solution is employed for recalcification than with tenth molar as directed in the paper.

We prefer the method of thromboplastin preparation described in 1936<sup>53</sup> to the later method employing acetone extraction,<sup>61</sup> because of the greater stability of the resulting product.

For sources of error in prothrombin determination, Aggeler, P. M., and Lucia, S. P.: *Proc. Soc. Exper. Biol. & Med.* 39: 11, 1935; and Stewart, J. K., and Pohle, F. J.: *Ibid.* 38: 532, 1935, should be consulted.



# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## THE RELATION OF VITAMIN K TO THE HEMORRHAGIC TENDENCY IN OBSTRUCTIVE JAUNDICE, WITH A REPORT ON CEROPHYL AS A SOURCE OF VITAMIN K

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VITAMIN K was discovered by Dam in 1934<sup>10</sup> as a new accessory food factor required for the normal development of chicks. Since withdrawal of the vitamin from the diet of the common laboratory mammals produced no symptoms, the attention of physicians was not directed to it until 1938 when three separate groups of investigators<sup>15, 22, 31</sup> showed that it could be successfully used to combat the hemorrhagic tendency in obstructive jaundice.

It now appears that this entity, which has puzzled physicians and surgeons so long, is merely another conditioned deficiency, a deficiency of vitamin K conditioned by the absence of bile salts from the intestinal tract. In the absence of bile salts vitamin K is not absorbed in adequate amounts from the intestine.

It is impossible to review the discovery and development of vitamin K without simultaneously considering some of the work on the hemorrhagic tendency in jaundice. This subject has been developed in two directions. On the one hand, attempts have been made to devise a test to detect the hemorrhagic tendency preoperatively. Bleeding time, clotting time, serum calcium concentration, fibrinogen concentration, prothrombin time by the method of Howell,<sup>43</sup> and sedimentation rate as recommended by Linton<sup>50</sup> were tried and found unreliable. The Ivy bleeding time,<sup>44</sup> the clotting index of Bancroft, Kugelmass, and Stanley-Brown,<sup>11</sup> and the clot volume index of Boyce and McFetridge<sup>12</sup> were proposed later and are still being tried.

On the other hand, attempts were made to treat the hemorrhagic tendency both prophylactically and therapeutically. Calcium was given by mouth and intravenously, high carbohydrate diets and intravenous glucose therapy were recommended, and pre- and postoperative transfusions were tried. This subject was reviewed by Ravdin and Johnston<sup>64</sup> and by Ivy, Shapiro, and Melnick.<sup>45</sup> An evaluation of

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TABLE I

PROTHROMBIN ESTIMATIONS OF PLASMA FROM PATIENTS WITH OBSTRUCTIVE JAUNDICE WHEN THEY HAD HEMORRHAGIC PHENOMENA

AUTHOR	DIAGNOSIS	PRO- THROMBIN PER CENT OF NORMAL	PRO- THROMBIN TIME (QUICK) (SECONDS)	COAGULATION TEST OF DAM AND GLAVIND
Brinkhous, Smith, and Warner	1. Carcinoma of pancreas	37		
	2. Cholangitis; abscess of head of pancreas	23		
	3. Cholangitis?	34		
	4. Carcinoma of pancreas	17		
	5. Common duct stones	16		
	6. Carcinoma of biliary tract	10		
Dam and Glavind	7. Carcinoma			Decreased coagulability (same) Normal coagulability
	8. Cholelithiasis			
	9. Cholelithiasis			
Quick	10. Common duct obstruction due to an adhesion	2.5		
Butt, Snell, and Osterberg	11. Carcinoma head of pancreas		95	
	12. Carcinoma head of pancreas		170	
	13. Carcinoma common duct		105	
	14. Carcinoma hepatic duct		75	
	15. Stricture of common duct		70	
	16. Carcinoma head of pancreas		60	
	17. Cirrhosis of liver		48	
	18. Carcinoma head of pancreas		180	

Dam and Lewis<sup>27</sup> concentrated vitamin K 1,100 times from dried alfalfa and Almquist obtained it as a crystalloid.<sup>3</sup> Osterberg<sup>53</sup> has described a method of concentrating it from fish meal. Thayer, MacCorquodale, Binkley, and Doisy<sup>74</sup> report obtaining it in crystalline form. The melting point of the crystals is 69° C. Its chemical composition has not been reported.

The discovery of the vitamin followed independent investigations of a hemorrhagic disease of chicks by Dam in Denmark and Almquist in this country. On certain diets adequately supplied with other vitamins, chicks develop hemorrhages into subcutaneous tissues, skeletal muscles, and the gizzard. This phenomenon was noted by Dam<sup>17, 18</sup> in 1929, by McFarlane, Graham, and Richardson<sup>53</sup> and McFarlane, Graham, and Hall<sup>52</sup> in 1931, and by Holst and Halbrook<sup>42</sup> in 1933. That the disease was caused by the lack of a new accessory food factor was recognized by Dam,<sup>19</sup> Dam and Schönheyder,<sup>28</sup> and Almquist and Stokstad.<sup>7</sup> The designation K (Koagulations) was suggested by Dam.<sup>20, 21</sup>

the unknown plasma in a standard time interval with the concentration required to clot normal plasma in the same interval.

Probably the most accurate test for prothrombin is that of Warner, Brinkhous, and Smith.<sup>82</sup> In this procedure the prothrombin is first converted quantitatively to thrombin and the concentration of the resulting material required to clot a fibrinogen solution in a standard time interval determined. These authors also investigated the influence of antithrombin and showed that it was not an important factor in the hemorrhagic tendency in jaundice. It should be emphasized that all of these methods depend on the addition of thromboplastin.

Brinkhous, Smith, and Warner<sup>14, 81</sup> demonstrated a prothrombin deficiency in certain jaundiced patients and Dam and Glavind<sup>22, 25</sup> corroborated this finding. The percentage of jaundiced patients who bleed is not great, but the evidence that those who do bleed have a diminished prothrombin concentration is rather convincing (Table I).

There is general agreement that normal blood contains an excess of prothrombin. Quick<sup>61</sup> states that no serious bleeding is observed from prothrombin deficiency until its concentration sinks to below 10 per cent of normal. Brinkhous, Smith, and Warner<sup>14</sup> cite one case that exhibited a hemorrhagic tendency with a prothrombin concentration of 34 per cent. Little change is found in the coagulation time by the usual methods until prothrombin concentration has fallen to 15 per cent of normal.<sup>61</sup>

Quick<sup>61</sup> states that relatively few jaundiced patients have a reduced prothrombin concentration. In 43 patients with obstructive jaundice whose plasma was studied in the Harrison Department of Surgical Research the prothrombin time was significantly prolonged in over 40 per cent.

A reduction in the prothrombin concentration may also occur in patients with external biliary fistulas as demonstrated by Brinkhous, Smith, and Warner.<sup>14</sup> Hemorrhagic phenomena in a patient with this condition were previously described by Judd, Snell, and Hoerner<sup>47</sup> and a similar case was encountered by Ravdin.<sup>63</sup>

#### VITAMIN K

Vitamin K, which was discovered by Dam<sup>17, 19</sup> while studying sterol metabolism in chicks, is a fat-soluble vitamin. Dam found it in the non-sterol easily saponifiable fraction of hog liver fat. It is readily soluble in ether, hexane, and hot methyl alcohol (50° C.). It may be precipitated from the latter solvent by chilling. It vaporizes between 120° and 145° C. in vacuo. Its chemical characteristics have been investigated by Dam and his co-workers<sup>20, 29</sup> and very extensive studies have been carried out by Almquist<sup>1, 2, 4, 5</sup> and by Klose, Almquist, and Meechi.<sup>48</sup>

by Dam and Glavind<sup>25</sup> in one rabbit. The deficiency was relieved by administration of K and produced a second time.

The intravenous injection of concentrated preparations of the vitamin into K-avitaminotic chicks was reported by Dam, and co-workers<sup>26</sup> who were able to restore the coagulability of the blood to normal in five hours, and later by Ansbacher,<sup>10</sup> who was able to restore the prothrombin concentration of the chicks' plasma to normal levels in two and one-quarter hours. Intramuscular injection was effective, but a longer period was required.<sup>26</sup>

Before vitamin K was successfully used in the treatment of prothrombin deficiency in the jaundiced patient, considerable experimental data on the relation of abnormalities of the biliary tract to blood coagulation had accumulated which served as an important guide to the clinical application of the vitamin. In 1935 Hawkins and Whipple<sup>41</sup> produced hemorrhagic phenomena in dogs by complete biliary fistulas. Hawkins and Brinkhous<sup>40</sup> showed that those hemorrhagic phenomena were due to a prothrombin deficiency using the technique of Warner, Brinkhous, and Smith.<sup>52</sup> Quick<sup>60</sup> suggested that the lack of bile salts in the intestine might interfere with the absorption of vitamin K. Greaves and Schmidt<sup>38</sup> produced prothrombin deficiency in the rat by bile fistulas and by ligation of the common duct. They further demonstrated that the deficiency could be corrected by giving enormous doses of vitamin K or by giving small doses of the vitamin along with bile salts.

Vitamin K, like vitamin D, is a fat-soluble material and is in turn dissolved by fat solvents. It had previously been shown by Greaves and Schmidt<sup>39</sup> that vitamin D was poorly absorbed in the absence of bile salts and their later paper<sup>38</sup> made it apparent that bile salts played a major role in the absorption of vitamin K.

Smith, Warner, Brinkhous, and Seegers<sup>72</sup> demonstrated that the prothrombin deficiency in bile fistula dogs could be relieved by the administration of alfalfa and bile salts. This explains the success of Judd<sup>46</sup> and Wangenstein<sup>79</sup> in preparing jaundiced patients for operation by feeding bile preoperatively, a method to which too little attention was given. Recently animal bile desiccated in vacuo has been used by Johnston<sup>44</sup> and Winfield<sup>83</sup> preoperatively in certain biliary tract cases.

Clinical success in treating jaundiced patients who showed a prothrombin deficiency by the oral administration of vitamin K and bile salts was reported by Warner, Brinkhous, and Smith<sup>51</sup> and by Butt, Snell, and Osterberg,<sup>15</sup> from the Mayo Clinic.

Intramuscular administration of K concentrates has been employed successfully in patients by Dam and Glavind<sup>22</sup> and by Butt, Snell, and Osterberg<sup>16</sup> at the Mayo Clinic. These latter authors found the method inferior to the oral method of administration which they

The distribution of the vitamin was studied by Dam<sup>20, 23</sup> and by Almquist<sup>7-9</sup> and their co-workers. Hog liver fat, putrified fish meal, alfalfa, kale, spinach, and hemp seed were found to be excellent sources. Egg yolk is a fair source, especially if the laying hen has been given a diet rich in vitamin K.<sup>8</sup> Cod liver oil, unpolished rice, wheat germ oil, lemon juice, and yeast were poor sources.

Dam and Glavind<sup>23</sup> showed that the vitamin was abundant in peas germinated in the light but not in those germinated in the dark and showed that there was little deterioration of the K content of leaves upon withering.

The presence of the vitamin in the feces of animals was shown by Almquist and Stokstad,<sup>8</sup> and Dam and Glavind<sup>22</sup> report its presence in the feces of man after seven days on a K-free diet. Almquist, Pentler, and Mecchi<sup>6</sup> showed that several common bacteria appear to contain the vitamin even when grown on K-free media. Among these are the colon bacillus and the *Staphylococcus aureus*. Diets free of vitamin K have been described by Dam<sup>19, 21, 28</sup> and by Almquist and Stokstad.<sup>7, 8</sup> Almquist diets have been used in most of the work in this country.

Methods of assay have been developed by Dam,<sup>21</sup> Dam and Schönheyder,<sup>29</sup> Dam and Glavind,<sup>24</sup> Almquist and Stokstad,<sup>7</sup> Thayer, McKee, MacCorquodale, and Doisy,<sup>75</sup> Ansbaeher,<sup>10</sup> and Dam.<sup>32</sup> Both preventive and curative methods have been employed. Thus far all assays have been carried out on chicks.

Dam has employed a unit defined as the least amount of vitamin K per gram of chick per day capable of producing normal coagulability in the blood of a K-avitaminotic chick after three days' feeding<sup>70</sup> and has used a dried spinach preparation as a standard.<sup>22</sup>

The cause of the hemorrhagic disease which develops in K-avitaminotic chicks was studied by Dam, Schönheyder, and Tage-Hansen.<sup>31</sup> They reported a coagulation defect due to a lack of prothrombin and showed that this factor returned to normal after the administration of foods which were rich in vitamin K. This finding was confirmed in this country by Quick,<sup>59</sup> who studied chicks given an Almquist diet. Thayer, McKee, MacCorquodale, and Doisy<sup>76</sup> suggested that the vitamin K may have a specific effect in curing the anemia of K-avitaminotic chicks apart from the fact that the loss of blood is stopped. This is denied by Almquist;<sup>9</sup> the evidence does not appear certain.

Attempts to produce hemorrhagic phenomena in other species by diet have been only partially successful.<sup>30</sup> The duckling and the gosling developed the disease. Pigeons and canaries showed some evidences of it, but it could not be produced in rats,<sup>6</sup> guinea pigs, or dogs by dietary means alone. A mild K-avitaminosis was developed

\*J. D. Greaves since has reported producing a K deficiency in 12 of 77 rats by a K deficient diet (Am. J. Physiol. 125: 429, 1939).

adapted for experimental work in which it is important to exclude the effects of vitamins A, B<sub>1</sub>, B<sub>2</sub>, and C.

The four bile salt preparations used, desicol, bilron, decholin, and sodium deoxycholate, all appear to be effective in appropriate dosage. Sodium deoxycholate is probably the most effective per unit of weight.

Except for the case mentioned by Quick<sup>61</sup> and two cases mentioned by Butt, Snell, and Osterberg,<sup>16</sup> all previously reported cases of prothrombin deficiency treated with vitamin K have responded satisfactorily. In our first patient (O. S.) the cause of failure was probably an insufficient dose of bile salts. In the case of R. P. vomiting and poor cooperation in taking the vitamin preparation undoubtedly resulted in a smaller net intake than the amount ordered. In the case of E. W. we have been unable to explain the poor response. It is possible that with a pure injectable preparation of vitamin K more uniform results might be obtained. In none of our patients, however, has serious hemorrhage occurred.

The mode of action of vitamin K has not been fully explained. The presumption, of course, is that it is a necessary building stone for the formation of prothrombin. This latter material, however, has never been isolated and like complement is known only by its function. In fact, it was thought for a time that the two might be identical, but they were differentiated by their reaction to aluminum hydroxide (Quick<sup>50</sup>) and to toluidine blue (Wising<sup>84</sup>).

Certain types of liver poisons produce a prothrombin deficiency. Smith, Warner, and Brinkhous<sup>71</sup> reported that chloroform anesthesia would reduce the prothrombin concentration in dogs very markedly within twelve hours. This has been confirmed by Quick<sup>61</sup> and in studies being made in this department. Similar results are said to follow the administration of phosphorus<sup>82</sup> and carbon tetrachloride.<sup>61</sup> Ether anesthesia is said to be without effect.<sup>26</sup>

Another method of producing a prothrombin deficiency is to feed animals spoiled clover hay. The hemorrhagic disease resulting from ingestion of this material is known among veterinarians as sweet clover disease and the nature of the dyscrasia was demonstrated by Roderick.<sup>68</sup> It is readily cured by feeding alfalfa, though it is doubtful whether this is due to the vitamin K content of the latter as Quick<sup>59</sup> found it to be effective even after ether extraction.

Recent investigations of the mode of action of vitamin K have been reported by Dam and co-workers.<sup>26</sup> They showed that K in highly concentrated form did not contribute in vitro to coagulability of blood or plasma from K-avitaminotic chicks even after contact for considerable periods. They were able to show that removal of the spleen did not alter the response of K-avitaminotic birds to the vitamin. The unexpected finding that exclusion of the liver from the circulation (in geese) was followed by improved blood coagulability according

employed.<sup>15</sup> They demonstrated that the oral administration of vitamin K without bile salt did not increase the prothrombin concentration in a case of obstructive jaundice but that a slow increase could be obtained in a patient with this condition by the administration of normal bile with a normal diet.<sup>15</sup>

More detailed reports on the clinical use of vitamin K have been published by Brinkhous, Smith, and Warner<sup>14</sup> and by Snell, Butt, and Osterberg.<sup>16, 73</sup> The material used and the results obtained are summarized in Table II.

TABLE II

REPORTED INSTANCES OF THE TREATMENT OF PROTHROMBIN DEFICIENCY IN JAUNDICED PATIENTS WITH VITAMIN K AND BILE SALTS

AUTHORS	NO. OF PA-TIENTS	SOURCE OF VITAMIN K	BILE SALT	RESULTS
Warner, Brinkhous, and Smith <sup>14</sup> Brinkhous, Smith, and Warner <sup>14</sup>	4	Extract of alfalfa	Human bile and sodium taurocholate	Prothrombin returned to normal in each case
Butt, Snell, and Osterberg <sup>15</sup> Snell, Butt, and Osterberg <sup>73</sup> Butt, Snell, and Osterberg <sup>16</sup>	17*	Extracts of fish meal and alfalfa	Animal bile salts of several varieties	Prothrombin was controlled in 15 instances; 2 patients died with hemorrhage; some vitamin K was given intramuscularly
Dam and Glavind <sup>22</sup> Dam and Glavind <sup>25</sup>	5	Extract of alfalfa	0	Blood coagulability by the method of these authors returned to normal in all cases
Quick <sup>61</sup>	1	Alfalfa	?	Ineffective

\*These authors treated 60 patients with obstructive jaundice. How many of these were treated prophylactically without a prothrombin deficiency is not stated. From cases cited, it is evident that at least 17 cases treated had a prothrombin deficiency.

Fourteen additional cases of prothrombin deficiency in jaundiced patients studied in the Harrison Department of Surgical Research are presented. These patients were treated in four Philadelphia hospitals. Details of the therapy used and the results obtained are given in Table III. The prothrombin times were determined according to the method of Quick<sup>58, 62</sup> and for the sake of uniformity are recorded with reference to the normal controls.

The source of vitamin K was a preparation of dried young cereal plants (oats and wheat) made by the Cerophyl Laboratories, of Kansas City, Mo., and marketed under the name of cerophyl. This preparation has been assayed by Elvehjem,<sup>33</sup> who found that it would protect chicks when added to a K-free diet in the proportion of 1:400. It is a greenish powder easily ingested in capsules or in tablet form. It can also be taken as a powder shaken up in fruit juice or tomato juice. It contains several other vitamins and consequently is not

adapted for experimental work in which it is important to exclude the effects of vitamins A, B<sub>1</sub>, B<sub>2</sub>, and C.

The four bile salt preparations used, desicol, bilron, decholin, and sodium deoxycholate, all appear to be effective in appropriate dosage. Sodium deoxycholate is probably the most effective per unit of weight.

Except for the case mentioned by Quick<sup>61</sup> and two cases mentioned by Bntt, Snell, and Osterberg,<sup>16</sup> all previously reported cases of prothrombin deficiency treated with vitamin K have responded satisfactorily. In our first patient (O. S.) the cause of failure was probably an insufficient dose of bile salts. In the case of R. P. vomiting and poor cooperation in taking the vitamin preparation undoubtedly resulted in a smaller net intake than the amount ordered. In the case of E. W. we have been unable to explain the poor response. It is possible that with a pure injectable preparation of vitamin K more uniform results might be obtained. In none of our patients, however, has serious hemorrhage occurred.

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RESULTS OF THE TREATMENT OF PATIENTS WITH PROTHROMBIN DEFICIENCY BY CEROPHYL (VITAMIN K) AND BILE SALTS

TABLE III  
HARRISON DEPARTMENT OF SURGICAL RESEARCH

PATIENT AND DIAGNOSIS	PROLONGATION PROTHROMBIN TIME BEFORE TREATMENT (% OF NORMAL)	THERAPY	PROLONGATION PROTHROMBIN TIME AFTER TREATMENT (% OF NORMAL)	RESULT
O. S. Carcinoma of pancreas	4,000	Cerophyl, 5.0 gm. Desicol, 1.0 gm. Cerophyl, 25.0 gm. Desicol, 3.0 gm. Transfusion	4,000	Hemorrhage into a biopsy wound Patient died
S. L. Carcinoma involving common duct	300	Cerophyl, 7.0 gm. Bilron, 2.0 gm. Transfusion, cholecystgastrostomy	200	Recovered No hemorrhage
P. S. Common duct obstruction due to stone	20	Cerophyl, 7.0 gm. Bilron, 2.0 gm.	Normal	Operated upon No hemorrhage
N. K. Common duct obstruction Small hemorrhage	40	Cerophyl, 15.0 gm. Decholin, 2.0 gm.	Normal	A slight hemorrhage had occurred after cholecystostomy
After K was stopped, fresh bleeding occurred	30	Cerophyl, 15.0 gm. Decholin, 4.0 gm. or Bilron, 2.0 gm.	Normal	No further hemorrhage
		Cerophyl, 15.0 gm. Decholin, 2.0 gm.	Normal	

SURGERY

TABLE III—CONT'D

I. P. Liver abscesses	80	Cerophyl, 15.0 gm. Bilron, 2.0 gm.	} daily for 3 days followed by a few smaller doses of sodium deoxycho- late	30	No hemorrhagic phenomena; vomiting made the administra- tion uncertain
E. W. Catarrhal jaundice	60	Cerophyl, 15.0 gm. Bilron, 2.0 gm.	} daily for 3 days	60	Recovered without hemorrhagic phenomena; the vitamin ap- peared to have no effect
G. Z. Stricture of common duct; slight hemor- rhage on eighth post- operative day	40	Cerophyl, 15.0 gm. Bilron, 2.0 gm.	} daily for 9 days	Normal	No further hemorrhage
K. G. Obstructive jaundice	40	Cerophyl, 15.0 gm. Bilron, 2.0 gm.	} daily for 6 days	Normal	No hemorrhagic phenomena; op- eration refused
R. P. Obstructive jaundice	150	Cerophyl, 15.0 gm. Sodium deoxycholate, 0.6 gm.	} daily for 5 days	150	No hemorrhagic phenomena; op- eration refused
P. Obstructive jaundice	30	Cerophyl, 15.0 gm. Sodium deoxycholate, 0.6 gm.	} daily for 7 days	Normal	No hemorrhagic phenomena
N. Obstructive jaundice	60	Cerophyl, 15.0 gm. Bilron, 2.0 gm.	} daily for 1 day	50	Operated upon 2 days later; no postoperative hemorrhage
S. Obstructive jaundice	30	Cerophyl, 7.5 gm. Bilron, 2.0 gm.	} daily for 10 days	Normal	No hemorrhagic phenomena
Biliary fistula	1,200	Cerophyl, 10.0 gm. Bilron, 2.6 gm.	} daily for 3 days	Normal	Patient was bleeding from ears and gums before treatment
Baby K. Hemorrhagic disease of the newborn	600	Cerophyl, 2.5 gm. Bilron, 0.6 gm.	} daily for 1½ days	Normal	Patient had been bleeding from cord and nose 24 hr. before first prothrombin determination but bleeding stopped following a transfusion given before these determinations.

to the method of Schönheyder<sup>70</sup> prevented a satisfactory evaluation of the role of the liver. The increased coagulability was attributed to a decrease in antithrombin.

Partial hepatectomy carried out by Warner<sup>69</sup> resulted in a decrease in prothrombin concentration which could be correlated to some extent with the amount of liver removed.

The present hypothesis on the relation of vitamin K to the hemorrhagic tendency in jaundice may be summarized as follows: The hemorrhagic tendency in jaundice is due to a deficiency in plasma prothrombin which in turn is due to a K avitaminosis which in turn results from absence of bile salts from the intestinal tract. Absence of bile salts may occur without obstruction of the common duct for it has been repeatedly shown that bile from the liver after obstruction may contain no bile salts and that these salts may not reappear in the bile until many days after the obstruction has been relieved.<sup>65, 77</sup> Prolonged clotting time has been observed by Walters<sup>78</sup> in a patient with carcinoma of the liver who showed no jaundice and it seems probable that a prothrombin deficiency will be found in certain patients with liver injury of various types not associated with jaundice. Patients with complete biliary fistulas may develop a hemorrhagic diathesis and a prothrombin deficiency<sup>81</sup> even though they show no jaundice. Whether the liver damage which occurs in obstructive jaundice decreases prothrombin directly or whether it does so solely through its effect on bile salts is an unproved point. Of course, the evidence that the liver is the chief source of prothrombin is not complete though the recent paper of Warner<sup>80</sup> strongly supports this contention.

Two sets of observations indicate that the absence of bile salts in the intestinal tract may not be the sole factor in producing the prothrombin deficiency. One is the fact that doses of vitamin K and bile salts adequate to correct a prothrombin deficiency promptly in most instances may have very little effect in an exceptional case (Table III, Case E. W.). The other is the fact that, although bile fistula dogs in which no bile gains access to the intestinal tract require two to three months to develop a prothrombin deficiency, dogs receiving liver poisons, such as chloroform anesthesia, develop such a deficiency in a few hours.

Hepatic damage incident to the use of anesthetics in general use has been shown by Rosenthal and Bourne,<sup>69</sup> using the bromsulphthalein test, and more recently by Boyce,<sup>43</sup> using the hippuric acid conjugation test of Quick, and by Gray, Bntsch, and McGowan<sup>37</sup> in common duct cases, using the bile salt concentration of hepatic bile as the indicator. The results of the latter two studies are substantially at variance, but both studies show that demonstrable hepatic injury can follow anesthesia. It is noteworthy that in the report by Boyce,

which showed substantial injury with spinal anesthesia, the blood pressure was not controlled so that liver anoxemia may have developed. Goldschmidt, Ravdin, and Lucké<sup>36</sup> have shown that severe liver injury may even follow ether anesthesia if liver anoxia occurs.

On the basis of the data available, it is not possible to establish the mechanism of the action of vitamin K in detail. It appears probable that the amount of vitamin absorbed is not the only factor that may result in a prothrombin deficiency but that liver damage from various causes may do so also. Furthermore, Lichtman and Chambers<sup>49</sup> have described a sterol fraction of hog liver fat which has the power of curing the hemorrhagic disease of chicks but which differs chemically from K. Until confirmation of this work appears, it is difficult to evaluate this finding.\*

#### SUMMARY

It now seems certain that the hemorrhagic tendency in jaundice is associated with a decrease in plasma prothrombin and that vitamin K when administered orally with bile salts is usually effective in correcting it.

The best test for the hemorrhagic tendency in jaundice is prothrombin determination by one of the methods using an excess of thromboplastin. The method of Quick,<sup>58, 61</sup> while perhaps not the most exact, is probably the most practical for the clinical laboratory.

All patients with obstructive jaundice should have prothrombin determinations performed before operation. Operation should be deferred, if possible, if the prothrombin concentration is decreased.

Usually the oral administration of vitamin K and bile salts will restore prothrombin deficiencies to normal in a few days. The occasional case will respond less satisfactorily, but whenever possible the drugs should be continued, if necessary in increased dosage, until the prothrombin concentration has returned to normal.

In the presence of actual hemorrhage or if operation must be performed in the presence of a low prothrombin concentration, fresh blood transfusions may be relied upon to supply prothrombin directly.<sup>61</sup> Blood from "blood banks" is not recommended because its prothrombin content is usually decreased.<sup>67</sup> The prothrombin concentration may fall rapidly in the postoperative period<sup>16</sup> and for this reason it is wise to follow it closely during this time.

As vitamin K therapy is inexpensive, it is probable that it will be used routinely in patients with obstructive jaundice both before and after operation even though no prothrombin deficiency is found. By

\*Almquist and Klose (J. Am. Chem. Soc., 61: 745, 1939) recently have reported a combination of a potent preparation of vitamin K with deoxycholic acid. When this combination is broken down, the resulting product appears to be highly purified but does not have the characteristics of the crystals with vitamin K potency reported by Thayer et al.<sup>61</sup> It appears possible therefore that K is not a single substance but a group of substances with the same activity.

to the method of Schönheyder<sup>70</sup> prevented a satisfactory evaluation of the role of the liver. The increased coagulability was attributed to a decrease in antithrombin.

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this means the frequency with which indications for transfusion arise may be reduced.

Routine administration of vitamin K does not as yet avoid the necessity of prothrombin determinations as the response to the oral administration of vitamin K and bile salt is not uniform.

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## Book Reviews

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**Plastic Surgery.** By Arthur J. Barskey, M.D., Beth Israel Hospital, New York City. Cloth. Pp. 355, with 432 illustrations. Philadelphia, 1938, W. B. Saunders Company. \$5.75.

This small monograph on plastic methods in surgery is an eminently practical book. In 355 pages, profusely illustrated with suitable drawings and photographs, the author discusses the phases of surgery which fall within the special province of plastic surgeons. The principles involved in the use of free skin grafts, flaps, and pedicles are discussed well. The transfer of fascia and its practical applications is well done. However, no mention of its use in hernia operations is made.

The author prefers the classification of Veau to that of Davis and Ritchie in clefts of the lip and palate. The author uses also the somewhat unanatomic designation of harelip. In connection with the discussion of lipectomy, no mention is made of lipemia which attends operation occasionally or the danger of embolism.

Plastic operations upon the bowel, penis and scrotum, undescended testis, and kidney pelvis are not discussed.

There is one chapter on restorative aspects of orthopedic surgery and concluding chapter on prostheses. Well-selected bibliographies accompany each chapter.

The book can be recommended highly as a useful and practical text.

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**Anus, Rectum and Sigmoid Colon.** By Harry E. Bacon, M.D., Temple University, Philadelphia, Pa. Cloth. Pp. 600, with 487 illustrations. Philadelphia, Pa., 1938, Lippincott Company. \$8.50.

The author's object in writing this text has been "to place within the reach of all divisions of the medical profession a comprehensive and readily intelligible exposition of our present knowledge of the various affections of the anus, rectum and sigmoid colon." In his introductory foreword Lockhart-Mummery, of London, states: "Medical text-books are of two kinds. Those which express the opinions of a single man and those which more closely resemble an encyclopedia and give a comprehensive survey of all views. . . ." Whereas the author of this text does speak out of his own experience, he has followed his objective quite closely and has chosen to summarize the opinions of men whose statement is believed to be authoritative. In the main, the author has done this well; there are times, however, when the author details one opinion after another, so superficial in concept that entire omission of these shallow notions would have spared the reader needless irritation. Authors owe something to their readers in not repeating everything they hear or see.

The alleged causes of hemorrhoids enumerated are really ridiculous, yet the author does not deem the upright position important enough an etiologic agent to mention it.

The author's treatment of the surgical aspects of cancer of the pelvic colon and rectum is unusually well done and these chapters are also very well illustrated. A comprehensive list of references follows each chapter. The orderly plan in which the subject matter is discussed will find favor with readers. There is much to praise in this splendid volume and little to criticize.



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reviewing this chapter many times. An anesthetist should make himself so familiar with this chapter that he should have it flash through his mind each time he proposes to do a spinal anesthesia.

The physical laws involved in the technique and the physiology of the nervous system are also well discussed. The practical consideration of these points cannot be overlooked by the anesthetist who intends to have success in spinal anesthesia.

A large portion of the book reviews the drugs and techniques of the author and many other anesthetists, and describes in a new concise manner their agent, technique, and the results. The author usually gives his comment at the end of each description.

If the description of degrees of respiratory depression and the treatment of such depression, as described on page 210 and following, were intimately familiar to every practicing physician, many unnecessary deaths occurring from other causes than spinal anesthesia might be prevented.

The failures, difficulties, dangers, complications and sequelae, advantages and disadvantages, indications and contraindications for spinal anesthesia are well presented. The author's comments and the quoted comments of other anesthetists are well worth reviewing.

For the beginner, it is a book from which he would gain considerable knowledge of the subject. For the experienced anesthetist, the book is a very good though incomplete compilation of the literature on spinal anesthesia. It is to be highly recommended for anyone doing spinal anesthesia.

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**Diagnostik und therapeutische Indikationsstellung bei den chirurgischen Erkrankungen der Harnorgane.** By Professor Dr. Peter Janssen, Dusseldorf. Paper. Pp. 316. Berlin, 1938, Julius Springer, Publishers. R.M. 15.

As the author states in the preface, this book is intended as a guide to clinical urology largely for the use of the student and the general practitioner, and the book serves the intended purpose very well. In no sense should it be regarded as a comprehensive treatise on the subject of urology, but as a guide to the clinical application. Its practical nature is illustrated even in the pages devoted to anatomy of the various portions of the urinary tract, which are written with a view to clinical and therapeutic application. The discussions of diagnostic methods employed are excellent and are very evidently based on wide experience.

Among the best chapters are those devoted to injuries of the urethra and bladder. They are apparently based on the experience which the author obtained in the World War and in industrial surgery. A thorough description of the pathologic complications and treatment of these lesions is included.

The book illustrates the differences in opinion held by American and German urologists concerning some of the lesions observed in the urinary tract. Viewed from a therapeutic and surgical standpoint, many of the observations are hardly up to the standards set by American urology. The discussion of the treatment of urinary infection does not include all recent developments and no mention is made of modern chemotherapy and its various ramifications. The author fails to mention transurethral drainage of abscesses involving the prostatic ducts. He does not mention the grading of tumors of the bladder. In the treatment of tumors of the bladder, transurethral methods and cystectomy are not discussed. He regards the treatment of diverticula of the bladder as being always surgical and fails to recognize the fact that transurethral removal of obstruction of the bladder neck will suffice in most cases to overcome the diverticulum.

The lymph follicles have probably more to do with the origin of cryptitis than the author allows. He believes that establishing colostomy on the lower portion of the pelvic colon will eliminate prolapse, when, as a matter of fact, prolapse may concern the proximal or distal loop of the colostomy. The author favors the operation of presacral neurectomy for congenital megacolon; whereas, those who have had the most experience with sympathectomy for Hirschsprung's disease feel that it is inadequate. The author unfortunately omits all discussion of the items of diverticulae of the pelvic colon and acute obstruction due to malignancy, rather serious omissions in a book which essays to treat of the diseases of the sigmoid colon. The favorite prescriptions of well-known proctologists which occupy many pages could better have gone without mention.

Despite the failings that have been referred to, this text is without question one of the better books written by proctologic surgeons within recent years. It should prove valuable as a source book to general practitioners, surgeons, and proctologists.

*Röntgendiagnostik der gelenke mittels doppelkontrastmethods.* By J. Oberholzer, M.D., Bircher's Clinic, Aarau, Switzerland. Paper. Pp. 128, with 134 illustrations. Leipzig, 1938, Georg Thieme. Rm. 23.

Kleinberg advocated inflation of joints with oxygen as early as 1921 for roentgen study. The method, however, has not had an important vogue in this country. The author, who writes from Bircher's Clinic in Aarau, Switzerland, lends the very definite impression that the injection of negative (gaseous) as well as positive (opaque) media into joints for diagnostic purposes enjoys wide usage throughout continental Europe. The author says in his introduction that in Bircher's Clinic alone more than 2,000 joint injections have been made during the last eight years.

From the illustrations shown, one would infer reasonably that the method has real value, particularly in demonstrating objectively internal derangement of the knee joint, such as a torn meniscus or severed cruciate ligaments. The author says he could not inject the hip joint successfully on the cadaver for roentgen purposes, but finds it a feasible procedure in the living patient.

Anyone interested in improving diagnostic accuracy in joint disease will find this little monograph helpful.

*Spinal Anesthesia.* By Louis H. Maxson. Foreword by W. Wayne Babcock. Cloth. Pp. 409, with 69 illustrations. Philadelphia, 1938, J. B. Lippincott Company. \$6.50.

Medical literature is already overcrowded with references to spinal anesthesia; nevertheless, a justifiable contribution is made by Maxson (1) in offering a good exposition of the principles upon which good practice must be based; and (2) in describing a variety of techniques, followed by his own experience and critical judgment.

It is unfortunate that the untimely death of the author in October of the year of publication has deprived medical literature of further contributions from his pen.

The book reviews fairly thoroughly the history of spinal anesthesia, beginning in 1891 up to the present time. It describes in detail many of the different means of control of the anesthetic agent, when it is injected into the spinal canal.

His description of the anatomy involved in spinal anesthesia is considered from a practical viewpoint. Any doctor of medicine would not waste his time by

TABLE I  
RESULTS, DELAYED VS. IMMEDIATE OPERATION

AUTHOR	CASES	DEATHS	MORTALITY PER CENT
<i>Immediate Operation:</i>			
Stanton <sup>3</sup>	113	13	42.00
Doughty <sup>4</sup>	7		28.60
Gardner <sup>5</sup>	122		18.00
Taylor and Schmidt <sup>6</sup>	61		16.40
Easton and Watson <sup>7</sup>	100	12	12.00
Guerry <sup>8</sup>	94	10	10.64
Reid et al. <sup>9</sup>	2,921		6.30
Pattison <sup>10</sup>	1,211	62	5.20
Schullinger <sup>11</sup>	2,653	135	5.08
Potter <sup>12</sup>	200	9	4.50
Hobler <sup>13</sup>	2,260		4.30
King <sup>14</sup>	364		4.20
McLanahan (in children) <sup>15</sup>	179		3.91
Sprague et al. <sup>16</sup>	1,463		2.73
Nuttall <sup>17, 18</sup>	551		2.50
Gile and Bowler <sup>19</sup>	901		1.89
Herrick <sup>20</sup>	217	5	1.84
Bliss and Heaton <sup>21</sup>	2,100	10	0.47
<i>Delayed Operation:</i>			
Taylor and Schmidt <sup>6</sup>	33		15.20
Doughty <sup>4</sup>	7		14.30
Kehl and Rentschler <sup>22</sup>	126	16	12.60
Coller and Potter <sup>23</sup>	85	8	9.40
Gardner <sup>5</sup>	126		8.70
Stanton <sup>3</sup>	83	7	8.50
Holder and Wells <sup>24</sup>	1,031		8.20
Pool <sup>25</sup>	757	45	5.94
Sperling and Myrick <sup>26</sup>	518	29	5.06
Arnheim and Neuhoof <sup>27</sup>	332	18	5.40
Kirtley and Daniel <sup>28</sup>	1,000		5.10
Garlock <sup>29</sup>	433	20	4.60
Bunch and Doughty <sup>4</sup>	2,309		2.29
Guerry <sup>8</sup>	135	2	1.40
Ochsner and Percy <sup>30</sup>	1,000	22	2.20
Augustana Hospital	3,771	83	2.20
Authors <sup>7</sup>	303	4	1.30

them together in a naturally defensive reaction. With a preponderance of streptococci, the fibrin is often very scanty with little or no agglutination of opposing surfaces. The fibrin forms a protective covering and together with the omentum limits the spread of the infection. This protective mechanism may be broken down by various foreign forces resulting in the spread of the infection. One of the chief methods by which bacteria are disseminated over the surface of the peritoneum is by peristaltic movement of the intestine. This peristalsis is excessive following ingestion of food or cathartics. Cessation of peristalsis is a protective phenomenon and occurs concomitantly with the peritoneal changes. With the occurrence of this protective adynamic ileus, there is little danger of the breaking down of adhesions and spreading the infection. Excessive dilatation of the intestine must be prevented, however, if intramural compression of the vessels

dicitis, there would be slight need to discuss the indications for any other treatment. Unfortunately, however, far too many patients with acute appendicitis are first seen by the surgeon after extension of the infection has occurred. It is in this large group of cases with acute appendiceal peritonitis that the conservative treatment is indicated. That there is a definite field for the treatment of appendiceal peritonitis is demonstrated by a consideration of the number of cases of acute appendicitis admitted to the hospital after extension of the infection beyond the appendix has already occurred. Ochsner, Gage, and Garside<sup>1</sup> in a review of a group of consecutive cases of acute appendicitis admitted to the Charity Hospital in New Orleans, La., found that at the time of admission in 78.7 per cent of the cases the infection extended beyond the appendix. Finney's<sup>2</sup> analysis of 1,807 cases of acute appendicitis revealed that in 37.5 per cent there was spreading of the infection upon admission to the hospital.

The original conception of the treatment of acute appendicitis was that of immediate operation regardless of the progress of the inflammation or of the existence of complications. No other treatment was considered feasible until A. J. Ochsner advocated deferred operation in certain indicated cases. The discussion continues between the advocates of the delayed operation and the immediate operation, each group reporting almost equally good results with its plan of management in a selected group of cases (Table I).

The unfavorable results obtained by those who have endeavored to follow the conservative treatment of appendiceal peritonitis can be attributed largely to a misunderstanding of the cardinal principles originally proposed by A. J. Ochsner. Many have interpreted the Ochsner treatment as being the conservative treatment of acute appendicitis. Nothing could be further from Ochsner's original concept. It was for acute appendiceal peritonitis that Ochsner first advocated the conservative treatment. This plan of treatment is based upon a correct evaluation of the reaction of the peritoneum to bacterial irritants. Peritonitis begins as a local lesion, which may remain thus or which may spread and become diffuse. At first the peritoneum simply appears pinker and more injected than normal. Then the normal sheen is lost, owing to the deposition of a thin layer of fibrin on the surface, which acquires a frosted or ground-glass appearance. Microscopic examination shows the usual appearance of an inflamed serous membrane. The fluid exudation is excessive. The exudate consists mainly of fibrin threads with a variable number of leucocytes and a few red blood cells. The amount of fibrin deposited depends somewhat upon the infecting organism. When colon bacilli predominate, a thick matting is often deposited on the coils of intestine, binding

month intervals. In this series of 48 dogs, 28 survived, 15 of which were treated conservatively and 13 by immediate operation. The average mortality for the entire series of 48 dogs was 42 per cent. The mortality according to degree of appendiceal damage was 12.5 per cent, mild; 52 per cent, moderate; and 80 per cent, severe damage. In the group with mild damage there was no mortality for the conservatively treated dogs, whereas a mortality of 33.3 per cent was recorded for those dogs operated upon immediately. In the group with moderate damage a mortality of 42 per cent resulted from conservative treatment and of 60 per cent from radical surgical treatment. All dogs treated conservatively in the group with severe damage died, and three-fourths of those treated by operation succumbed. The total mortality following the conservative treatment was 29 per cent and following immediate surgical treatment was 52 per cent. From these results Schmidt and Taylor<sup>35</sup> concluded that the conservative treatment causes a lower mortality than the operative treatment. They also found that most of the deaths were due to generalized peritonitis (65 per cent), and that the occurrence of adhesions in the peritoneal cavity was more than doubled by operative procedure and drainage.

The original report of the Ochsner treatment came from the Augustana Hospital. These statistics at the time of their first publication appeared revolutionary and their authenticity was at first questioned. Subsequent observations have shown, however, that the early statistics reported by Ochsner could not be considered as unusual, and, after more experience with the plan of management, Ochsner definitely improved on his first results.

There have been no reports in recent years from the Augustana Hospital indicating the present status of the treatment that Ochsner originally outlined. With the refinement in treatment now available, better results should be expected and some modification is justifiable. Advance in therapy should be credited to the Wangensteen continuous duodenal suction and to the availability of more satisfactory intravenous solutions. These measures were not used by Ochsner. He did not give fluids intravenously or subcutaneously but placed much dependence on nutrient enemas. Consequently, excessive dehydration not infrequently existed. This has been more definitely explained since McNealy and Willems<sup>36</sup> and Ebeling<sup>37</sup> have demonstrated the futility of depending upon absorption from the rectum of any fluids other than tap water. We have also found that duodenal suction is preferable to intermittent gastric lavage from the standpoints both of efficiency in decompressing the upper gastrointestinal tract and of convenience and comfort of the patient. With minor exceptions, however, the plan of management, as outlined by Ochsner, has been followed by us and other staff surgeons at the Augustana Hospital.

is to be avoided. This defensive mechanism may terminate in any one of three ways: Localized infection in the peritoneum may end by resolution without suppuration; adhesions may keep the inflammation strictly limited and localized suppuration occur; or the infection may spread diffusely.

Ochsner reasoned that the natural protective reaction of the peritoneum could be further enhanced by directing treatment toward the inhibition of peristalsis in order to prevent the spread of infection. This physiologically sound argument is the basis of his whole method of treatment. The cardinal principles in this method as employed by Ochsner<sup>31, 32</sup> may be briefly enumerated: absolute prohibition of anything whatsoever by mouth; the employment of gastric lavage to combat distention of the intestine; the administration of retention enemas every three to four hours to carry on nutrition; the injection of morphine to relieve pain (and, Ochsner thought, also to retard peristalsis); and the administration of normal saline solution and glucose by proctoclysis to overcome dehydration. The patient is kept in the Fowler position, and absolute rest is essential. There must be no relaxation whatsoever in this treatment until the patient has been free from pain and fever for at least four days. It should be remembered that Ochsner recommended this regime only as a preparation for operation.

Following the proposal of A. J. Ochsner<sup>33</sup> for the delayed operation, many men became ardent advocates of this plan of management. Important among these advocates is Guerry, who lent considerable impetus to the Ochsner treatment. He<sup>s</sup> reports a series of 94 cases of gangrenous ruptured appendicitis with diffuse peritonitis, which were operated upon immediately. There were 10 deaths, a mortality rate of 10.64 per cent. In a similar series of 135 cases treated by the deferred operative method as advocated by Ochsner, the number of deaths was reduced to 2, a mortality of 1.4 per cent. In Guerry's<sup>34</sup> series of 2,959 consecutive cases, there were 16 deaths (a mortality rate of 0.54 per cent). Guerry attributes this comparatively large reduction in mortality percentage to the employment of the Ochsner method of treatment in the group of cases with appendiceal peritonitis.

Considerable experimental work has been done in an effort to determine the efficacy of the various methods of combating acute appendicitis. A recent report was made by Schmidt and Taylor<sup>35</sup> of research which they undertook in order to compare the conservative and radical methods of treatment. They made a study of 48 dogs in which they produced appendiceal damage of mild, moderate, or severe degree in an attempt to reproduce experimentally the condition of acute appendicitis. These dogs were examined at one-, two-, or three-

in a more serious form during childhood. Gangrene of the appendix is observed much earlier in children (and in the aged) and, because of the underdevelopment of the omentum, little localization occurs and diffuse contamination of the peritoneum rapidly ensues. A factor which increases the seriousness of the condition is the difficulty with which a diagnosis is made due to the lack of cooperation from the patients and the "typical" atypical character of the disease in the very young. Cathartics, which so often unwisely are given to children with vague abdominal symptoms, serve to aggravate an already perniciously grave condition. Many authors<sup>5, 15, 27, 30, 39, 42-45</sup> advocate immediate operation in children with acute appendicitis regardless of the stage of the disease, although Coller and Potter<sup>23</sup> express the opinion that the delayed method should be employed in children with peritonitis because they feel that any treatment would be essentially the same. Ochsner<sup>46</sup> believes that the conservative treatment would save many lives if employed in those cases with a beginning localization, regardless of age.

During the past seven years, we have seen 29 cases of acute appendicitis in children under the age of 13 years. Immediate operation was always done if the inflammatory process was confined to the appendix or had become definitely localized. In our series there were 18 cases operated upon immediately. If we believed that localization was beginning after the infection had extended beyond the appendix, conservative treatment was instituted whenever possible. A prolonged period of conservative treatment has been, in our experience, unsatisfactory. In these cases of children with acute appendicitis with perforation the average interval before operation was performed was 3.8 days, which is, of course, much less than the period of conservative treatment in adults. In children who are sufficiently cooperative to allow the use of intravenous infusions and duodenal suction conservative treatment can be employed satisfactorily, and in our opinion it should be used whenever possible in the presence of diffuse appendiceal peritonitis.

Deaver,<sup>47</sup> an enthusiastic advocate of Ochsner's method, preferred to refer to this treatment as "regulation," by which he meant strict anatomic and physiologic rest. His outline of treatment deviated only slightly from Ochsner's original plan. He advocated rest of the body by placing the patient in the Fowler position, either with the use of pillows or preferably with the aid of mechanical beds. Small doses of morphine for pain, stomach lavage, nothing by mouth, and employment of the Murphy drip contribute to rest of the alimentary canal. He also approved of ice applied to the abdomen to benumb the nerves of the walls of the abdomen. This treatment, however, was reserved for diffused peritonitis. In early cases of acute appendicitis before



Ochsner<sup>30</sup> made a study of 1,000 consecutive cases of appendicitis which were operated upon at the Augustana Hospital during the thirty-three months from July 1, 1901, to April 1, 1904. The total mortality for the series was 2.2 per cent. The mortality rate, according to classification, is more enlightening and is shown in Table II. Of these 255 patients in the second group, 200 were operated upon immediately after entering the hospital and 55 received the delayed treatment. In Group 3, 21 had immediate operations and 34 were treated by the delayed method. There were 39 immediate operations in Group 4 and 78 received the Ochsner treatment. All of the 33 cases with diffuse peritonitis received the deferred operative treatment. An analysis of the 22 deaths as given by the author reveals some interesting facts: Ochsner believed that all 3 deaths in the first group could have been avoided had the operation been confined to the removal of the diseased appendix. All 5 of the second group were operated upon immediately, and the author expressed the opinion that had they received the delayed treatment 3 and possibly 4 of these fatal cases could have had favorable terminations. Only 1 of the 4 deaths in Group 4 was avoidable, and that was a case in which the appendix was removed when only drainage of an abscess should have been undertaken. The other 3 deaths were due to "murderous use of cathartics," "probable thrombus of the external iliac vein," and "probable infarct due to a thrombus."

TABLE II  
MORTALITY IN OCHSNER SERIES ACCORDING TO CLASSIFICATION

TYPE OF CASE	CASES	DEATHS	%
1. Chronic appendicitis or interval operation	540	3	0.5
2. Acute appendicitis without perforation	255	5	1.9
3. Acute appendicitis perforated or gangrenous with abscess	55	0	0.0
4. Acute appendicitis perforated with abscess	117	4	3.4
5. Acute appendicitis with diffuse peritonitis	33	10	30.0

It should be noted here that Ochsner realized the limitations of this method of treatment, as he did not advocate its use in children or in the aged. He observed that old people do not seem to tolerate confinement in bed for any length of time. He felt that the chief reasons for restricting the employment of this method in children were the difficulty of following such a rigid treatment and the lack of sufficient development of the omentum to act as a protection.

The treatment of appendicitis in children requires a slightly different procedure. Most authors<sup>28-31</sup> have agreed that the disease is expressed

of abdominal operation for other conditions. In these cases, classified as chronic appendicitis, the appendix was the major surgical indication for the operation. In this series of chronic appendicitis there were no deaths.

There were 143 cases of acute appendicitis which we treated by immediate operation. The average interval between the onset of symptoms and operation was thirty-eight hours. It was our opinion that deferred operation was not indicated in these cases. It is unfortunate that many surgeons have established a rule for employing conservative treatment based on the duration of appendicitis. This is indeed a mistake. Every case of acute appendicitis presents a different problem, and it is impossible to formulate a plan of treatment based solely on the number of hours since the onset of the attack. Some of these 143 cases had been ill with appendicitis for four or five days. In many of these cases the inflammatory process in the appendix had progressed to the gangrenous stage, and in some there was free fluid in the peritoneal cavity. We have always performed immediate operation in those cases in which the appendix has only recently ruptured, and because no attempt at localization preceded or followed the perforation the appendix continues to contaminate the peritoneal cavity. In these cases there are no adhesions and consequently no danger of further disseminating the process by operation. Drainage was employed in only 5 cases in this group of 143. It is, of course, obvious that drainage need not be used in those cases in which the infection is limited to the appendix. The impossibility of draining the peritoneal cavity *per se* has been repeatedly demonstrated. In the many instances in which free exudate was encountered in the peritoneal cavity no attempt was made to establish drainage. The peritoneum, as has been said above, is able to withstand bacterial trauma very well indeed. In most cases, after removal of the appendix, the exudate is absorbed and spontaneous resolution occurs. In only 1 case which was closed without drainage, did a residual abscess occur. This abscess became localized in the cul-de-sac of Douglas and was easily drained through the rectum. We have noted, however, that in these cases with free peritoneal exudate a subcutaneous abscess may develop in the wound even though we make every effort to prevent contamination of the abdominal wall. For this reason a small rubber tube drain is placed in the wound just down to the fascia and is removed after two or three days.

The question of drainage has probably aroused as much interest as the discussion on the treatment of appendicitis. From a brief survey of the literature,<sup>56-60</sup> the pendulum appears to have swung from "when in doubt, drain," to "when in doubt, don't drain." Willis and Morn<sup>61</sup> briefly reviewed the opinions of earlier writers on drain-

the onset of peritonitis, immediate operation should be performed.<sup>48</sup> Deaver<sup>49</sup> pointed out that three signals which demand immediate operation are chill, abatement of pain, and drop in temperature.

A brief mention of the results obtained by Deaver and Magoun<sup>50</sup> in 5,488 appendectomies performed at the Lankenau Hospital of Philadelphia for the twenty-year period from 1900 to 1920 will be indicative of the effectiveness of this plan of treatment. There were 327 deaths, or a mortality of 5 per cent, in the entire series of cases. A detailed analysis of the mortality for five-year periods is further evidence of the value of the deferred method. The average mortality for the first five-year period from 1900 to 1905 was 10.5 per cent. All of these cases were operated upon immediately. From 1906 to 1909 the mortality was reduced to 5.6 per cent. Some of these cases were treated expectantly. From 1910 to 1920, when all spreading peritonitis cases were treated by the "regulation" method, the mortality was reduced to approximately 4 per cent. Keyes<sup>51</sup> reported a mortality rate of 7.3 per cent in 315 cases of perforated appendicitis with abscess formation; whereas in 98 cases of ruptured appendicitis with diffuse peritonitis the mortality rate was 27.5 per cent. Potter and Coller<sup>52</sup> report that when immediate operation was done in cases with appendiceal peritonitis the mortality rate was 52 per cent, and 21 per cent in those not actually moribund on admission. By employing the conservative treatment, the mortality in cases with peritonitis has been reduced to 8.6 per cent and to 5.6 per cent in cases with abscess. These statistics, together with those reported by Guerry, show a decided reduction in mortality with the advent of the Ochsner method of treatment.

In contradistinction to the enthusiasts<sup>53-55</sup> of the delayed operation many surgeons favor immediate operation regardless of the progress of the spread of infection or the condition of the patient. At operation the infected region is walled off from the rest of the peritoneal cavity by suitable placing of moist packs, and the appendix is removed. Drainage is instituted whenever it seems desirable. Among the advocates of the immediate appendectomy may be listed Herriek,<sup>20</sup> Nuttall,<sup>17, 18</sup> Reid and co-workers,<sup>9</sup> Gile and Bowler,<sup>19</sup> Hobbler,<sup>13</sup> King,<sup>14</sup> etc. They report mortality rates from 0.47 per cent to 42 per cent (Table I).

During the period from October, 1931, to October, 1938, we have treated 303 cases of appendicitis. Of this number, 107 were classified as chronic appendicitis. In some of these 107 cases other abdominal organs were the site of pathologic changes necessitating surgical treatment, but in all of these cases the appendix was chronically inflamed and definitely diseased. No mention is made in this series of those cases in which the appendix was removed incidentally during the course

ulcer. As concerns the postoperative condition with relation to the appendicitis, it seemed that the patient's progress was satisfactory.

During this same seven-year period we have treated 52 cases of complicated acute appendicitis by the deferred operative method. The average interval between the onset of symptoms and operation was 6.7 days. In all of these cases we considered the conservative treatment as outlined by Ochsner the method of choice, because it insured the patient the best prognosis as to mortality and morbidity. In only 1 case was the period of conservative treatment curtailed and operation performed in an attempt to prevent the spread of a partially walled-off appendiceal abscess. The patient's condition seemed to be growing rapidly worse and it was hoped that extraperitoneal drainage might be of some benefit. Details of this case follow:

CASE 2.—H. A., white male, 44 years of age, carpenter by trade, first examined in his home May 24, 1938, after having been acutely ill for seven days. Onset of illness was characterized by acute diffuse abdominal pain which the patient attempted to relieve by drinking a large quantity of ice water. This served to increase the pain, and in a further attempt to obtain relief he took several cathartics, including citrate of magnesia, castor oil, and Pluto water. Pain became continuously worse, and by the end of twelve hours became localized in the right lower quadrant. At this time the patient consulted a chiropractor who gave him several "adjustments." On May 20, 1938, three days after onset, the patient's condition seemed worse. He was unable to eat because of vomiting and suffered from abdominal distention. Chiropractic treatments were continued and catharsis was again employed. At the time of our first examination the patient appeared desperately ill. There was generalized abdominal tenderness with definitely more pain upon pressure over the right lower quadrant, where an indefinite mass could be palpated. Definite abdominal distention was present, with no evidence of peristalsis, and marked dehydration was shown by dry skin, parched lips and a high fever ( $103^{\circ}$ ). The patient was not able to retain anything by mouth and was restless and slightly delirious. He was admitted immediately to the hospital, and routine treatment for generalized peritonitis was instituted. Because of apparent slight improvement on the following day, it was hoped that localization would occur sufficiently to make operation safe within a few days. On this, his second hospital day, his temperature dropped to  $102.4^{\circ}$ . Large amounts of fluid were supplied intravenously, and with the reduction of dehydration the patient was considerably more comfortable. On the following day (third hospital day), however, his condition grew worse; abdominal distention increased in spite of continuous duodenal suction and his temperature again rose to  $103.4^{\circ}$ . It was thought that drainage of the localizing abscess, if accomplished without shock, might be beneficial. A McBurney incision was made close to the right iliac crest, the peritoneum lateral to the abscess was exposed, and eight Penrose cigarette drains were introduced into the lateral side of the abscess. An enormous amount of pus drained away immediately, and the previous treatment was continued. The patient's condition did not improve, the temperature continued to rise, and on the fourth day following institution of drainage death occurred.

At autopsy almost the entire peritoneal cavity was found to be filled with foul-smelling creamy pus. There were unsuccessful attempts at walling off this pus in several areas. The largest loculated collection was in the right lower quadrant in the appendiceal region. This cavity was being partially emptied by the Penrose

age and found that drainage seemed to have no effect on the mortality. From a study of 100 cases with drainage following operation for ruptured and gangrenous appendicitis, they concluded that drainage was unnecessary, as it did not subtract from the mortality but did add to the morbidity.

A history of catharsis was obtained in 20 cases. This history always suggests the possibility of early extension of the inflammatory process beyond the appendix. Therefore, in cases with a history of having taken cathartics, special attention is directed toward differentiating localizing peritonitis from generalized peritoneal involvement. No attempt is made here to record the many variations in the types of symptoms exhibited by these patients, because it would seem that nothing very beneficial could be obtained by reiterating these various trends of symptoms. The average duration of hospitalization post-operatively in these cases was nine days. There was 1 death in this series, an analysis of which follows:

CASE 1.—H. E. S., white male, aged 48 years, first seen at 9:30 P.M. upon admission to the hospital July 4, 1937, when he complained of pain and tenderness in the right lower abdominal quadrant. Nineteen hours previously he had first noted acute diffuse abdominal pain which he attributed to dietary indiscretion. About an hour after onset of pain he had a bowel movement, which he felt partially relieved his discomfort. He ate some breakfast with the result that there was recurrence of abdominal pain. He ate nothing during the remainder of the day and by evening had noticed that the pain had become localized in the right lower quadrant. He sought the advice of a physician who sent him immediately to the hospital. Upon admission, diagnosis of acute appendicitis was made, and immediate operation was performed. The appendix, which was found lateral to the cecum and adherent to the lateral abdominal wall, was purplish red in color and markedly swollen. It was sharply angulated in its mid-third by an adhesive band, and at this point gangrene was found. Considerable fluid exudate was present as well as plastic exudate over the appendix and cecum. Following appendectomy two cigarette Penrose drains were inserted. The next day his temperature rose to 103.4° but immediately fell to 100°. On the fourth day it dropped to 99.4° and on the fifth to 99°. Drainage through the Penrose drains was moderate, there was no abdominal distention, and by the fourth day there was a normal bowel movement and passage of considerable flatus. Early in the morning of the fifth postoperative day, while the patient was sleeping quietly, he awakened suddenly and vomited 100 c.c. of dark blood. Within a few minutes the patient was cold and clammy and the pulse rate, which was almost imperceptible, increased to 144. Immediately the patient was given a blood transfusion of 600 c.c. of whole blood. A Levine tube was passed and 650 c.c. of bloody fluid were aspirated. Dark red fluid continued to drain from the Levine tube constantly. Coagulin was administered, 50 per cent glucose was given through the Levine tube, and preparation was being made for another transfusion, but the patient died eight hours after the onset of hemorrhage. Permission for autopsy could not be obtained.

*Comment.*—We had previously treated this patient for a duodenal ulcer. It seems most plausible to consider that the few days of post-operative starvation served to accentuate the gastric hyperacidity and become a factor in causation of this fatal hemorrhage from the duodenal

this process can be greatly facilitated. This means of decompressing the upper intestinal tract assists also in relieving nausea or vomiting and in addition protects the intestine from the danger of excessive dilatation. Obviously catharsis will increase the spread of infection by stimulating peristalsis and will also retard localization by destroying limiting fibrinous adhesions. Because nothing can be given by mouth, fluids and electrolytes must be administered by some other route. Small amounts can be given by proctocolysis, but we rely almost entirely upon intravenous and subcutaneous administration. As a rule at least 3,000 c.c. of fluids are given daily. Almost routinely we use solutions of glucose and sodium chloride, given by intravenous injection.

In the administration of fluids we have been guided largely by the excellent work of Collier.<sup>63-65</sup> We owe much to the pioneer research of Collier and Maddock, whose study has placed the control of dehydration on a scientific basis. In 1936 they<sup>66</sup> undertook an intensive analysis of water metabolism in the sick and found that surgical patients lose about 2,000 c.c. of water by vascularization, and a minimum output of 1,500 c.c. of urine daily is necessary to insure adequate renal function. From these findings they deduced that patients who cannot take fluids by mouth require 3,500 c.c. of fluid daily. If the patient is losing fluid abnormally, as in vomiting, diarrhea, etc., provision should be made to replace this fluid loss also. They then studied a dehydrated patient and found that a patient in this condition weighing 60 kg. loses 3,500 c.c. of fluid. They estimated that a dehydrated patient should be given, in addition to the regular amount of fluid given a surgical patient, enough more to equal 6 per cent of the patient's body weight, or, for a 60 kg. patient, 3,600 c.c. plus 2,000 c.c. for vascularization and 1,500 c.c. for urine, or a total daily fluid administration of 7,100 c.c. In discussing the type of solution to be administered, Collier states that a saline solution should be given to replace fluid loss from the gastrointestinal tract and the remainder of the fluid should be 5 per cent dextrose in distilled water.

The patient should be placed in the Fowler position. We do this routinely to favor gravitation of the fluid exudate to the pelvis, for a residual abscess in the cul-de-sac of Douglas is much more readily diagnosed and treated than abscesses in the upper abdomen. Heat in some form should be applied to the abdomen. As a rule we use large hot fomentations together with a heat tent. If the weight of the hot fomentation causes any discomfort, the heat tent alone is used. There is evidence to show that heat aids in controlling distention by decreasing secretion in the intestine. Also abdominal pain seems to be relieved, at least somewhat, by the application of heat. Morphine should be given in fairly large doses. A. J. Ochsner originally used morphine because he believed it splinted the bowel. It has been shown

drains. In the center of this large abscess the appendix was found. It was completely gangrenous and had partially sloughed away. A considerable amount of pus was collected in the subphrenic and subhepatic areas. All the loops of small intestine were matted together with plastic exudate, and upon separation of these loops collections of pus were found. A large collection of pus almost equal in size to that on the right was found in the left iliac fossa. A large cul-de-sac abscess was continuous with the abscess on the right. Another significant finding was a beginning empyema of the left pleural space. Anatomic diagnosis established at autopsy was ruptured gangrenous appendicitis, generalized peritonitis with multiple localized collections of pus in the peritoneal cavity, hydrothorax, and early empyema of the left pleural cavity and parenchymatous degeneration of the liver.

*Comment.*—This case represents that unfortunate circumstance in which, after partial localization of an appendiceal abscess, further peritoneal spread ensues. It did not seem desirable to operate upon this patient when he was first seen, although some localization was present. Drainage was undertaken in a desperate effort to overcome the evident spreading of the original appendiceal abscess. The almost unbelievable extent of suppuration in the peritoneal cavity as seen at autopsy leads one to wonder why the patient lived even a few hours.

In all of these 52 cases delay had ensued before consulting us. Many had been treated injudiciously with cathartics and other home remedies. In every case the infection had extended beyond the appendix, and each one presented an individual problem as to treatment.

As a rule the defensive forces operative in the peritoneal cavity are at least partially successful in walling off an acutely inflamed appendix before perforation occurs. The omentum migrates to surround the inflamed viscus and fibrinous adhesions quickly form. A definite degree of localization, therefore, usually exists at the time perforation occurs. If these cases are first seen after perforation and at the beginning of localization, we believe that great harm will be done by immediate operation. If given an opportunity, complete localization will follow and resolution will even occur in many cases. If, however, the patient is seen only a few hours after rupture of the appendix into virgin peritoneum, immediate operation is done, as has been stated above. If this same type of case is seen later after localization is beginning conservative treatment should be instituted. Conservative treatment of appendiceal peritonitis is indicated in those cases seen "too late for an early operation and too early for a late operation."<sup>62</sup>

By conservative treatment of appendiceal peritonitis, attempt is made to assist the physiologic response of the peritoneum in limiting the spread of the infection and favoring localization. Normally, cessation of intestinal peristalsis will occur, and treatment can best be directed toward promoting this physiologic reaction. The presence of vomiting and reverse peristalsis usually serves to empty the upper intestinal tract. By duodenal drainage with a perforated catheter,

The performance of a primary cecostomy has been advocated by a number of surgeons for many years.<sup>7, 68-70</sup> In many of these difficult cases in which we found that, in spite of continuous duodenal decompression by the Wangenstein suction, the terminal ileum, cecum, and ascending colon were markedly distended, we have frequently inserted a catheter through the appendiceal stump after removal of the appendix. This cecostomy does not prolong the operation at all. We routinely remove the appendix by using the inversion without ligation technique.<sup>71</sup> This is the method that A. J. Ochsner introduced at the Augustana Hospital, and we have found no occasion to vary the technique. By this method the mesoappendix is first grasped with forceps, divided, and then ligated with fine catgut ligatures. Next, a purse-string suture of silk on a fine needle is introduced so as to include an intramural branch of the appendicular artery. This is accomplished by starting the purse-string suture from one side of the mesoappendix and passing it down to and including the submucosa, and bringing it out on the opposite side of the mesoappendix. The suture is then reinserted in exactly the same manner, thereby forming a loop around a segment of the cecal wall adjacent to the mesoappendix. This loop encircles any intramural branch of the appendicular artery and, after tightening the loop sufficiently to occlude the artery, the purse-string suture is continued around the cecum in the conventional manner. Next, three Ochsner clamps are applied to the base of the appendix, and, after walling off the area with moist sponges, the appendix is divided between the upper and middle forceps. We use a scalpel to section the appendix. There would be some advantage in using the thermocautery, but at the present time the type of anesthetic gas employed so frequently prevents the use of the cautery that we have continued to follow A. J. Ochsner's example of using only the scalpel. After the appendix is sectioned, a sponge is used carefully to wipe off the small amount of secretion on the middle forceps. The middle clamp is then removed and the crushed tip securely grasped with a pair of plain tissue forceps. Traction is then made upward on the fixed end of the purse-string suture and upward traction is also made on the cecal wall by grasping the tenial band with a toothed tissue forceps at a point opposite to the mesoappendix. The remaining Ochsner clamp is then removed and the stump of the appendix inverted into the lumen of the cecum by pushing it downward with the smooth tissue forceps. The purse-string suture is drawn tightly as the tissue forceps is gently freed and withdrawn. At this point, if a cecostomy is to be done, a 22 F catheter is passed through the lumen of the inverted stump and the purse-string suture tied securely. A second purse-string suture is then placed and the stump inverted further. This technique of cecostomy (Figs. 1-4), which was used in 35



conclusively, however, both clinically and experimentally<sup>67</sup> that morphine does not retard peristalsis but is beneficial because it increases the tone of the bowel and prevents excessive dilatation of the intestine with its concomitant intramural compression of the vessels.

It is a great satisfaction to observe the change in the patient's condition soon after conservative treatment is instituted. Abdominal distention diminishes, nausea and vomiting subside, pain decreases, the pulse improves, and the fever becomes lower. As localization progresses, usually a palpable mass can be outlined. Optimum time for operation must be chosen. Operation too early will disseminate infection from an imperfectly localized abscess, and operation too long delayed may in a few cases allow intraperitoneal rupture of a localized abscess. Frequently localized peritonitis may subside spontaneously. With the formation of an abscess, however, evidence of a septic process continues. The leucocyte count decreases but still remains above normal. Fever continues but is usually very slight except for an afternoon elevation. Drainage of the abscess is indicated and carries a very good prognosis. Unnecessary manipulation in an attempt to remove the appendix should be avoided. If the abscess has been well localized and gentle handling practiced, it is generally possible to remove the appendix without disseminating the infection. With but 4 exceptions in this series of 52 cases, the appendix was removed at the primary operation. In 3 of these cases the patient returned in a few months for an interval appendectomy, and the other patient died. The type of incision employed depended for the most part upon the site of the appendiceal abscess. We have found that the pararectus incision with a retraction of the rectus muscle medially allows adequate exposure of the right iliac fossa with a minimum destruction of important structures of the abdominal wall. This type of incision was used most frequently, although the McBurney incision was used in 5 instances. In addition to the limitation of exposure afforded by the McBurney incision, we believe that drainage is hampered somewhat by this gridiron type of incision. Upon opening the peritoneal cavity, utmost care is maintained to prevent soiling of uninvolved peritoneum. This is best accomplished by adequate exposure and the careful placing of gauze packs. Before opening the abscess the wound edges should be protected likewise to avoid undue contamination of the abdominal wall. With one exception Penrose drains were used. The incision is closed very loosely with interrupted sutures, and in a few instances in which it was deemed advisable to close the abdominal incision, little or not at all, iodoform gauze was placed just down to the peritoneum to prevent a herniation of intestine through the incision. This gauze was not used as a drain in any way and was removed after twenty-four hours.

The performance of a primary cecostomy has been advocated by a number of surgeons for many years.<sup>7, 68-70</sup> In many of these difficult cases in which we found that, in spite of continuous duodenal decompression by the Wangensteen suction, the terminal ileum, cecum, and ascending colon were markedly distended, we have frequently inserted a catheter through the appendiceal stump after removal of the appendix. This cecostomy does not prolong the operation at all. We routinely remove the appendix by using the inversion without ligation technique.<sup>71</sup> This is the method that A. J. Ochsner introduced at the Augustana Hospital, and we have found no occasion to vary the technique. By this method the mesoappendix is first grasped with forceps, divided, and then ligated with fine catgut ligatures. Next, a purse-string suture of silk on a fine needle is introduced so as to include an intramural branch of the appendicular artery. This is accomplished by starting the purse-string suture from one side of the mesoappendix and passing it down to and including the submucosa, and bringing it out on the opposite side of the mesoappendix. The suture is then reinserted in exactly the same manner, thereby forming a loop around a segment of the cecal wall adjacent to the mesoappendix. This loop encircles any intramural branch of the appendicular artery and, after tightening the loop sufficiently to occlude the artery, the purse-string suture is continued around the cecum in the conventional manner. Next, three Ochsner clamps are applied to the base of the appendix, and, after walling off the area with moist sponges, the appendix is divided between the upper and middle forceps. We use a scalpel to section the appendix. There would be some advantage in using the thermocautery, but at the present time the type of anesthetic gas employed so frequently prevents the use of the cautery that we have continued to follow A. J. Ochsner's example of using only the scalpel. After the appendix is sectioned, a sponge is used carefully to wipe off the small amount of secretion on the middle forceps. The middle clamp is then removed and the crushed tip securely grasped with a pair of plain tissue forceps. Traction is then made upward on the fixed end of the purse-string suture and upward traction is also made on the cecal wall by grasping the tenial band with a toothed tissue forceps at a point opposite to the mesoappendix. The remaining Ochsner clamp is then removed and the stump of the appendix inverted into the lumen of the cecum by pushing it downward with the smooth tissue forceps. The purse-string suture is drawn tightly as the tissue forceps is gently freed and withdrawn. At this point, if a cecostomy is to be done, a 22 F catheter is passed through the lumen of the inverted stump and the purse-string suture tied securely. A second purse-string suture is then placed and the stump inverted further. This technique of cecostomy (Figs. 1-4), which was used in 35

cases, is very simple and provides a serosal tract which quickly closes upon removal of the cecal catheter. The tip of the catheter is directed either into the cecum or through the ileocecal valve into the terminal ileum, the choice being established by the indication for decompression. This catheter is brought out through the abdominal wall by

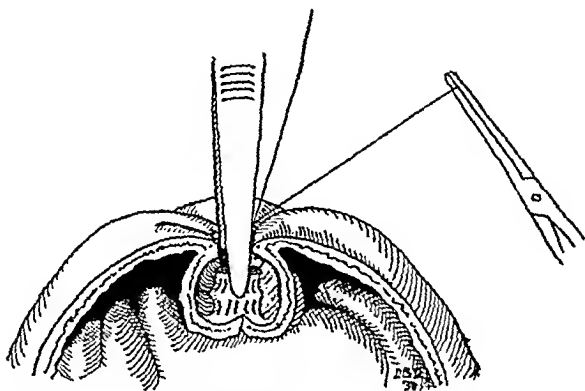


FIG. 1.—Appendiceal stump inverted without ligature, purse-string suture tightened slightly but not tied.

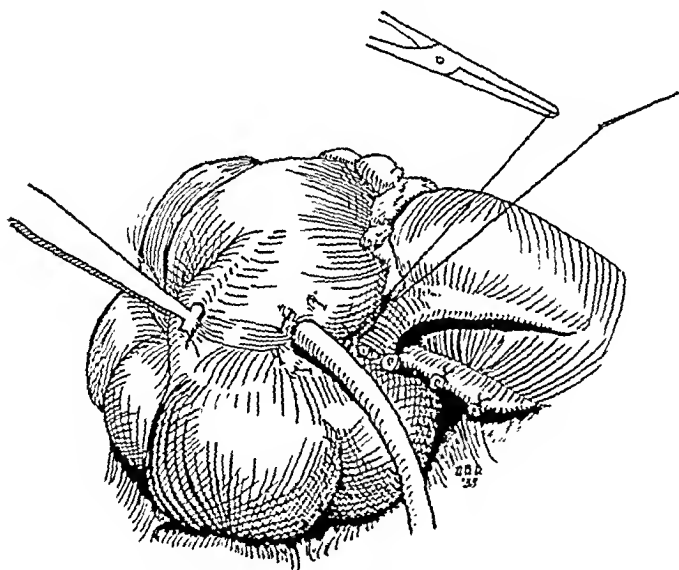


Fig. 2.—Catheter being pushed through lumen of inverted appendiceal stump.

means of a small stab wound which is so placed that the head of the cecum lies easily against the point of exit of the catheter. Through this catheter normal saline solution is injected at hourly intervals. By injecting saline, an opening in the catheter is assured, and, as a part of the solution will siphon away, drainage of fecal material and gas is facilitated. It is gratifying to note the absence of distention when

this type of cecostomy is used. The cecal catheter is removed usually after ten days (the average interval was 10.6 days in our series). Its use, however, does not replace duodenal suction, as this is employed concomitantly.

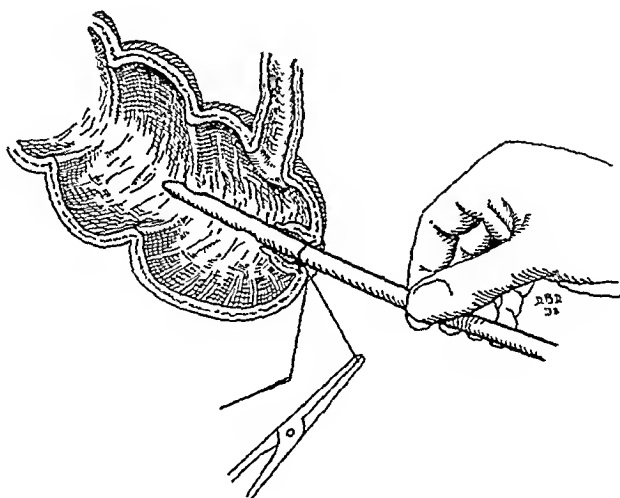


Fig. 3.—Catheter in cecum, first purse-string suture being tied.

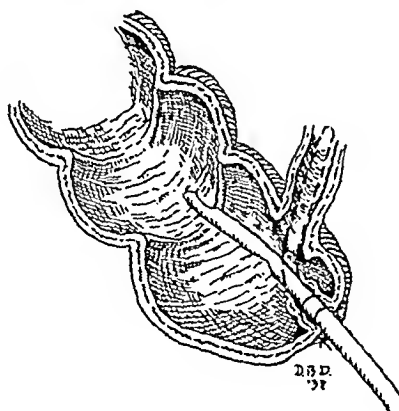


Fig. 4.—Second purse-string suture tied. Dotted outline shows alternate position of catheter in ileum.

According to Paine and Wangensteen,<sup>72</sup> Ward, of San Francisco, was apparently the first to treat postoperative distention by employing the principle of continuous suction in connection with the in-lying duodenal catheter. They<sup>72</sup> state, however, that Westermann<sup>73</sup> and Kappis<sup>74</sup> more than twenty-five years ago first advocated the use of the duodenal tube in the treatment of distention of peritonitis. The general technique of employment which has been described by Wangensteen and Paine<sup>73, 74</sup> is fairly simple: A small duodenal catheter of

the Levine type is passed through the nose into the stomach. A simple water siphon exerts constant suction (about 75 c.c. of water). Perforations are carried back on the catheter for about ten inches, which provide for simultaneous suction of both the stomach and duodenum when the tip of the catheter enters the duodenum. This prevents further vomiting.

Postoperative treatment is essentially a continuation of the conservative treatment used preoperatively. The patient is placed in the Fowler position or is turned to the right side if this best facilitates drainage. Adequate doses of morphine are given, and attention to water balance is observed, chiefly by the use of intravenous solutions of glucose and sodium chloride. As a rule heat in the form of a heat tent is kept constantly applied to the abdomen. The average duration of the postoperative hospital stay was 25.3 days. There were 3 deaths in this series of 52 cases of perforated acute appendicitis. An analysis of 1 has been given above and discussion of the other 2 cases follows:

CASE 3.—W. J., white male, 40 years of age, truck driver. Two days prior to admission the patient developed a "stomach-ache" characterized by a dull, dragging pain across the abdomen. The ingestion of some pills resulted in nausea and vomiting. The following day the pain localized in the right lower quadrant. The patient no longer vomited but suffered abdominal distention. Upon admission Jan. 25, 1932, the patient was placed on routine conservative treatment for three days. At this time there seemed to be sufficient evidence of localization to warrant operation. Accordingly, on the third hospital day an operation was performed. The appendix was gangrenous, filled with pus, and surrounded by omental and peritoneal adhesions. There was considerable free pus and free fluid in the abdomen. Appendectomy with primary cecostomy was done and two cigarette drains were inserted. Following the operation, the patient's temperature rapidly rose to 103°, his pulse became weaker, and he expired on the afternoon of the first postoperative day. No autopsy was permitted.

*Comment.*—This case came to operation too soon and should have been treated conservatively for a longer period of time before operation. When at operation it was seen that there was inadequate localization of the inflammatory process, nothing should have been done except the simple insertion of drains. Considerable free fluid containing plastic exudate was seen in the peritoneal cavity, and this already existing diffuse peritonitis was made more virulent by dissemination of the infection from the appendiceal abscess.

CASE 4.—C. Q., an obese male, 61 years of age, electrician, admitted to the hospital June 12, 1935. When the patient became ill one week previously, he thought he had a "cold in his stomach." During the illness he complained of nausea and anorexia, and consequently ate very little. For constipation he took a "physic" pill daily. Abdominal examination upon admission revealed a mass the size of an orange in the right lower quadrant. After conservative treatment for two days, operation was performed. A large appendiceal abscess was found well walled off in the right lower quadrant. The appendix, which was large, swollen,

and gangrenous, was removed and a catheter was inserted into the cecum through the appendiceal stump. Six cigarette drains were inserted into the appendiceal abscess. Routine postoperative treatment was instituted. The patient's immediate postoperative condition was good. On the first postoperative day the patient was doing rather well and there was no distention. On the second postoperative day the temperature became normal and the patient's condition appeared excellent. During the night of the third postoperative day, the patient had a chill, developed chest pains, became dyspneic, and had marked tachypnea and a nearly imperceptible pulse. The temperature rose at once to 102°. Coarse râles could be heard over the entire chest. The patient was placed in an oxygen tent and digitalis was given intravenously. Cyanosis became noticeable in spite of oxygen. By the fourth postoperative day the temperature had reached 105.6°. The pulse rate varied from 140 to 160. The heart was irregular, consolidation was evident in the bases of both lungs, and respiration was labored. Pulmonary edema increased and on the sixth postoperative day the patient died.

*Comment.*—This obese patient was an elderly alcoholic who developed a diffuse bronchopneumonia with rapidly increasing pulmonary edema and cardiac failure. Unfortunately autopsy was not allowed, but clinically it seemed that the abdominal condition was definitely improving at the time of onset of the pneumonia.

During the corresponding period of time represented by our series, there were treated at the Augustana Hospital 3,771 cases of appendicitis (Table III). Of this total number, there were 83 deaths, a mortality of 2.2 per cent. It is interesting to note the coincidence that the mortality percentage exactly corresponds to the percentage quoted by A. J. Ochsner in 1904 from the Augustana Hospital. The highest percentage of these deaths occurred, as would be expected, in acute appendicitis and in particular in those cases with perforation. There were 23 (19 per cent) deaths in this group. In general, the Augustana Hospital series parallels our series. It would be difficult to express an opinion concerning the extent of preoperative preparation in all of those which required delayed treatment. It would undoubtedly be found that a few were operated upon prematurely and incompletely prepared. In general, however, most of these patients were treated conservatively and with the exception of some modifications received routine Ochsner treatment. It is favorable to note the lowest percentages were met in 1937 and 1938. More adequate supervision and more careful preoperative preparation may accomplish a still further lowering of the mortality.

Of the 195 cases of acute appendicitis in our series, 143 cases had immediate operation and 52 patients were treated by the deferred operation. In the series treated by immediate operation, there was 1 death, a mortality of 0.69 per cent. In those cases that were operated upon at once, the infection in nearly every case was limited to the appendix. In a few cases extension had occurred so recently that no adhesions had formed. In the series treated by deferred opera-

the Levine type is passed through the nose into the stomach. A simple water siphon exerts constant suction (about 75 c.c. of water). Perforations are carried back on the catheter for about ten inches, which provide for simultaneous suction of both the stomach and duodenum when the tip of the catheter enters the duodenum. This prevents further vomiting.

Postoperative treatment is essentially a continuation of the conservative treatment used preoperatively. The patient is placed in the Fowler position or is turned to the right side if this best facilitates drainage. Adequate doses of morphine are given, and attention to water balance is observed, chiefly by the use of intravenous solutions of glucose and sodium chloride. As a rule heat in the form of a heat tent is kept constantly applied to the abdomen. The average duration of the postoperative hospital stay was 25.3 days. There were 3 deaths in this series of 52 cases of perforated acute appendicitis. An analysis of 1 has been given above and discussion of the other 2 cases follows:

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*Comment.*—This case came to operation too soon and should have been treated conservatively for a longer period of time before operation. When at operation it was seen that there was inadequate localization of the inflammatory process, nothing should have been done except the simple insertion of drains. Considerable free fluid containing plastic exudate was seen in the peritoneal cavity, and this already existing diffuse peritonitis was made more virulent by dissemination of the infection from the appendiceal abscess.

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tion, there were 3 deaths, a mortality of 5.7 per cent. These were all seen "too late for early operation." In all but 1 case in this series drainage was used. In 4 cases the appendix was not removed at the primary operation. In the series of 195 cases of acute appendicitis there was a mortality of 2.05 per cent. Contrary to the usual sex distribution there were more females than males in our series (106 and 89 respectively). The 4 deaths in our series occurred in men, a mortality of 4.5 per cent. The oldest patient with acute appendicitis was 72 years old and the youngest was 5 years of age. The greatest number of patients was in the second, third, and fourth decades, there being 59, 50, and 31 patients in these respective groups. There were 19 patients in the fifth decade, 3 of whom (aged 41, 46, and 48 years) died, a mortality of 15.9 per cent. In all, only 4 patients in the seventh decade were seen, and 1 of these died (a mortality of 25 per cent). The average leucocytosis met with in our series of acute appendicitis was 17,500 (15,200 in simple acute appendicitis and 19,900 in ruptured appendicitis). The red blood cell count was not remarkable, as would be expected, the average being 4,571,000. In the cases with simple acute appendicitis the average maximum temperature was  $99.8^{\circ}$ , with 6.3 days being the average febrile period; whereas, in the cases of acute ruptured appendicitis the average maximum temperature was  $102.5^{\circ}$  with an average febrile period of 19.2 days. This difference in febrile reaction in these two groups emphasizes somewhat the definite variation in the severity of the disease. In the more severe manifestation of the disease, a need for adequate exposure made us favor the use of a muscle retracting right rectus incision. In those cases treated by delayed operation, a McBurney incision was used only 5 times. One of these patients died as detailed above. A right rectus incision was made in the 3 other patients who died after being treated by delayed operation. When immediate operation is indicated, we have a tendency to favor the McBurney incision unless we anticipate a need for more than the usual exposure. Consequently, we have used the McBurney incision in 78 of the 143 cases of this series. In this immediate operation series the 1 patient who died had a right rectus incision.

#### COMMENT

We have reported this series of cases observed during the past seven-year period in order to review our results from the conservative treatment of acute appendiceal peritonitis. These results seem encouraging enough to justify the continuation of this type of management. From a review of the 4 deaths occurring in this series, it is probable that 1 of them resulted from inadequate preoperative preparation. This was undoubtedly due to misjudging the degree of localization present. It is reasonable to believe that this case could have



TABLE III  
MORTALITY ACCORDING TO YEARS IN AUGUSTANA HOSPITAL SERIES

APPENDICITIS	1931		1932		1933		1934		1935	
	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS
Chronic	308	7	325	10	334	4	327	5	269	0
Acute, simple	220	0	193	1	173	5	111	1	125	3
Acute, perforated with abscess	10	0	13	2	10	2	18	1	10	1
Acute, perforated with peritonitis	28	2	23	4	11	2	18	7	21	5
Total	656	9	554	17	528	13	474	14	428	9
Mortality (per cent) by years	1.37%		3.07%		2.46%		2.91%		2.10%	
Chronic	1936		1937		1938		TOTAL		MORTALITY %	
	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS		
Acute, simple	263	7	288	2	173	1	2407	36	1.49	
Acute, perforated with abscess	139	1	117	0	59	0	1140	11	0.96	
Acute, perforated with peritonitis	11	1	20	4	11	2	103	13	12.61	
Total	20	3	425	6	243	3	121	23	19.00	
Mortality (per cent) by years	2.77%		1.40%		1.23%		3.77%		2.2	

tion, there were 3 deaths, a mortality of 5.7 per cent. These were all seen "too late for early operation." In all but 1 case in this series drainage was used. In 4 cases the appendix was not removed at the primary operation. In the series of 195 cases of acute appendicitis there was a mortality of 2.05 per cent. Contrary to the usual sex distribution there were more females than males in our series (106 and 89 respectively). The 4 deaths in our series occurred in men, a mortality of 4.5 per cent. The oldest patient with acute appendicitis was 72 years old and the youngest was 5 years of age. The greatest number of patients was in the second, third, and fourth decades, there being 59, 50, and 31 patients in these respective groups. There were 19 patients in the fifth decade, 3 of whom (aged 41, 46, and 48 years) died, a mortality of 15.9 per cent. In all, only 4 patients in the seventh decade were seen, and 1 of these died (a mortality of 25 per cent). The average leucocytosis met with in our series of acute appendicitis was 17,500 (15,200 in simple acute appendicitis and 19,900 in ruptured appendicitis). The red blood cell count was not remarkable, as would be expected, the average being 4,571,000. In the cases with simple acute appendicitis the average maximum temperature was  $99.8^{\circ}$ , with 6.3 days being the average febrile period; whereas, in the cases of acute ruptured appendicitis the average maximum temperature was  $102.5^{\circ}$  with an average febrile period of 19.2 days. This difference in febrile reaction in these two groups emphasizes somewhat the definite variation in the severity of the disease. In the more severe manifestation of the disease, a need for adequate exposure made us favor the use of a muscle retracting right rectus incision. In those cases treated by delayed operation, a McBurney incision was used only 5 times. One of these patients died as detailed above. A right rectus incision was made in the 3 other patients who died after being treated by delayed operation. When immediate operation is indicated, we have a tendency to favor the McBurney incision unless we anticipate a need for more than the usual exposure. Consequently, we have used the McBurney incision in 78 of the 143 cases of this series. In this immediate operation series the 1 patient who died had a right rectus incision.

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been saved by awaiting further localization before operation or by limiting the procedure to simple drainage. One death (H. A., Case 2) occurred when a partially localized appendiceal abscess spread further, to cause a very extensive suppurative diffuse peritonitis. It is difficult to see how any type of treatment could have altered the outcome in this case. The other 2 deaths were caused by factors other than those directly due to appendicitis and might be expected to occur in any group of surgical cases.

In our series, as in nearly all other reports, the cases presenting the most difficulty in treatment were neglected cases that had received cathartics. As of course would be expected, many complications were encountered. Pylephlebitis occurred in 1 case and was the most serious complication met with in the patients who recovered. In 2 cases there was a rupture of a localized appendiceal abscess. One of these patients died. These complications will be completely discussed in a paper now in preparation.

Departure from routine Ochsner treatment consisted only in minor refinements in therapy. The introduction of duodenal drainage popularized by Wangensteen has been of great benefit in the treatment of abdominal distention so frequently encountered in complicated appendicitis. Cecostomy done at the time of operation has seemed to have been of further help in a few of the most desperate cases by aiding in the decompression of the lower small intestine, cecum, and ascending colon. Maintaining the fluid intake of these patients is more readily accomplished at this time than when Ochsner originally advocated this plan of treatment. We believe that far from being discarded the Ochsner treatment should receive further consideration and evaluation. If such is done, we feel certain that a more universal adoption of this plan of management will be made.

#### SUMMARY

1. A series of 303 cases of appendicitis are herein presented.
2. In 195 cases of acute appendicitis the principles of the Ochsner treatment were employed.
3. A plea is made for a review of the conservative treatment of appendiceal peritonitis.
4. In our series of 303 cases there were 4 deaths, a mortality of 1.3 per cent.

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# ACUTE APPENDICITIS, SIMPLE AND COMPLICATED

## A CRITICAL ANALYSIS OF 1,010 CASES TREATED AT THE ROBERT PACKER HOSPITAL

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IN AN editorial in *The American Journal of Surgery* for August, 1935, Guthrie expressed the opinion of thoughtful surgeons that most reported grouped statistics on appendicitis meant little because they were all-inclusive and varied depending principally upon the number of chronic, acute clean, or even secondary cases included in the series. It is evident that on a careful surgical service there will be only an occasional accidental death in those cases where the pathology is limited to the appendix per se. However, in the remaining cases in which the pathology has spread through perforation to the stage of local peritonitis, spreading or diffuse peritonitis, or abscess formation, the mortality will be necessarily high. It is by a careful study of these cases that the merits of various treatments and the skill of surgeons may be evaluated.

There have been several recent reports in which an honest attempt has been made to state a mortality in these complicated cases. The figures have been high. It is in the spirit of self-analysis that we are reporting a study of 1,010 cases of acute appendicitis handled on the surgical service of the Robert Packer Hospital during the five-year period from June 1, 1932, to May 31, 1937. Two hundred and sixty-six cases with the diagnosis of subacute appendicitis and 279 chronic cases operated upon during this period are not included. In an attempt to aid diagnosis, certain statistical compilations regarding symptomatology and findings in this group of cases are also reported.

Connell has recently suggested that for statistical study acute appendicitis cases be analyzed according to the following classification:

Acute	{ Nonperforated	{ Abscessed	{ Local
	{ Perforated		
		{ Peritonitis	{ Diffuse

Following this classification these 1,010 cases may be subdivided as shown in Table 1. It is evident that less than 20 per cent of the cases in the series make up the group of perforated cases in which, as will be shown, most of the mortality falls.

Predisposing Factors.—Before proceeding to a discussion of the mortality in this series, several predisposing factors of appendicitis and its

TABLE I  
GENERAL GROUPING

			NUMBER OF CASES	PERCENTAGE OF SERIES
Nonperforated	821	{ Acute	670	66.33
(81.28%)		{ Gangrenous	151	14.95
Perforated	189	{ Abscessed	68	6.78
(18.72%)		{ Local peritonitis	111	10.95
		{ Diffuse peritonitis	10	0.99
		Total	1010	100.00

complications and some information concerning the symptomatology of these cases are to be considered.

*Age.*—Although appendicitis may occur at any age, it is known to have its highest incidence in the "teens." As stated by Deaver: "The susceptibility of young persons to appendicitis is mainly due to the abundance of lymphoid tissue and the tendency to infection of all lymphoid tissue during adolescence and to the dietary indiscretions that are the privilege of youth." The average age for the series, calculated on a basis of 960 cases in which age was given, is 23.8 years. The average for simple acute cases is 21.6 years; for gangrenous, 27.7 years; for abscessed, 28.13 years; and for the local and general peritonitis group, 29.6 years. With an increase in the severity of the disease, there is an increase in the average age. Of more interest is the increased proportion of patients in the extremes of life; i.e., 6 years or under and 50 years or older in the complicated groups as compared to the simple acute cases as shown in Table II.

TABLE II  
INCIDENCE IN EXTREMES OF LIFE

	TOTAL NO. CASES	NUMBER 6 YR. AND UNDER	PERCENTAGE 6 YR. AND UNDER	NUMBER 50 YR. AND OVER	PERCENTAGE 50 YR. AND OVER
Acute	642	11	1.71	29	4.52
Gangrenous	134	6	4.48	19	14.18
Abscessed	68	6	8.80	13	19.11
Perforated with local or diffuse peritonitis	116	4	3.45	24	20.70

This tendency is shown even more clearly by graphs based on the five-year age groupings. The curve in simple acute cases reaches a high at 16 to 20 years and is very low in 0 to 5 and 51 plus groupings. In the complicated cases, including gangrenous appendicitis, the height of the curve is, of course, between 11 and 20 years, but the curve starts at a higher level and is maintained at a higher level in the older age groupings.

*Sex.*—Most reported series give a higher incidence of appendicitis in the male than in the female. This is true in our series which includes 529 males and 481 females. Deaver has emphasized the importance of

the better blood supply in the female afforded by the appendiculo-ovarian artery. This anatomic difference may be of even more significance in determining what happens to the patient who develops appendicitis.

TABLE III  
SEX GROUPING

	MALE	FEMALE
Acute	311	359
Gangrenous	102	49
Abscessed	43	25
Perforated	73	48
Total	529	481

It will be noted from Table III that the cases progressing to gangrene and perforation were predominantly male. Ten patients in the series had diffuse peritonitis, 9 of these were males. Of the 21 deaths in the series, 13 were males. It is likely that this greater tendency for males to develop complications is due not alone to anatomic differences, but also to a greater tendency to procrastination in seeking medical aid and continued physical exertion in the presence of developing appendicitis.

*Seasonal Incidence.*—It has seemed in the work of this clinic that there is some difference in the number of cases of appendicitis seen in the different seasons. The monthly incidence of cases is given under the diagnosis in Table IV.

It is shown that there is a definite increase in cases in the spring and summer. The total number of 531 cases from March 1 to Sept. 1 as compared with the 465 cases from Sept. 1 to March 1 shows an increased incidence during the warm months of about 15 per cent over the fall and winter.

TABLE IV  
SEASONAL INCIDENCE

MONTH	ACUTE	GANGRENOUS	ABSCESSSED	PERFORATED	TOTAL
January	65	6	5	15	91
February	57	10	9	11	87
March	57	18	4	10	89
April	64	13	10	7	94
May	60	12	3	7	82
June	75	16	2	11	104
July	42	14	9	15	80
August	56	14	10	16	96
September	48	12	4	7	71
October	58	15	4	9	86
November	53	9	2	6	70
December	35	12	6	7	60
Total	670	151	68	121	1,010

This coincides with the greater prevalence of gastrointestinal disorders during these seasons, and in the absence of a better explanation this will be assumed to be the cause.



TABLE V  
SEASONAL GROUPING

INCLUSIVE MONTHS	NUMBER OF CASES	
March-May	265	545
June-August	280	
September-November	227	465
December-February	238	

*Laxatives.*—In recent years the profession, and in more recent years the public, have been made cognizant of the role of laxatives in increasing the complications of appendicitis. Despite this fact, a careful history brings out the information that a large percentage of even the most recent cases in the series had laxatives. In this series 560 case histories gave definite information as to cathartic administration; 293, or over 50 per cent, had had one or more doses of laxative. The pioneer work of Bowes in publicity is certainly not in vain, but his message should be broadcast over the land. Even more tragic is the notation occasionally seen, "his physician gave him a laxative." Table VI brings out the fact that, whereas only 43 per cent of the simple acute cases had cathartics (in specified records), 60 per cent of the gangrenous had laxatives, and in cases in which the pathology had extended beyond the confines of this organ over 74 per cent had had laxatives. In other words, comparing the number of cases with laxative intake to those without in the simple cases, the ratio is 3:4; whereas in the perforated cases it is 3:1; or the proportion of perforated cases having laxatives is in the ratio of 4:1 as compared with the simple acute cases. This only further confirms the opinions already expressed that cathartics remove Nature's splint on the intestinal tract and increase dramatically the number of cases which go on to perforation.

TABLE VI  
LAXATIVE INCIDENCE

TYPE OF CASE	LAXATIVE	NO LAXATIVE	NOT SPECIFIED	PER CENT SPECIFIED WITH LAXATIVE
Acute	148	200	322	43
Gangrenous	54	36	61	60
Abscessed	37	10	21	78
Local peritonitis	48	19	44	72
Diffuse peritonitis	6	2	2	75
Total	293	267	450	52

*Time From Onset to Perforation.*—Undoubtedly another most important factor predisposing to complications of appendicitis is the increased time between the onset of symptoms and the operation. This is borne out in this study. Table VII demonstrates that the complicated cases were the ones with a longer average time between onset and operation.

The average time for the cases with confined pathology, i.e., acute and gangrenous, was about 36 hours. The time for perforated cases was figured with the exclusion of those cases in which delayed operation or no operation was performed, so the difference between 51 and 36, or 15 hours, is delay time pure and simple.

TABLE VII  
TIME UNTIL OPERATION

	NO. OF CASES WITH TIME GIVEN	AVERAGE TIME	LONGEST TIME	SHORTEST TIME
Simple acute	648	36.92 hr.	250 hr.	3 hr.
Gangrenous	144	33.00 hr.	240 hr.	3 hr.
Abscessed	66	13.1 days	35 days	30 hr.
Perforated with local or diffuse peritonitis	98	51.0 hr.	144 hr.	5 hr.

In this series this delay of 15 hours is the critical time during which, in the average case, perforation took place. The figures in the abscessed cases do not represent delay time in their entirety, since most of these patients were treated conservatively for a time to further localize the abscess. However, the time between onset and admission to the hospital was necessarily long, because at the time of admission it was considered that Nature had already, in part at least, walled off the infectious process.

#### SYMPTOMATOLOGY

It might be of some value in a review of a series of this size to analyze the common symptoms of appendicitis and its complications. Deaver states that: "Pain, tenderness and rigidity are the three cardinal symptoms of appendicitis; they are usually associated with vomiting, fever and leucocytosis." In this study the variables which could be most accurately evaluated from the charts have been considered. This includes the position of onset pain, admission temperature, leucocytosis, and differential. No attempt to analyze the degree of pain has been made because it is subjective and a statement of its quantity is not wholly dependable. No analysis of tenderness and rigidity has been made, not because they are not important, for they are most important, but because their evaluation introduces a personal equation and is likely to be inaccurate unless the same surgeon examined each patient, which was not the case.

The point of onset of pain is given by most authors as epigastric or periumbilical. This may be classical but by no means invariable. The incidence of the various points of onset is given in tabulated form (Table VIII) as noted by the physician taking the history. As would be expected, there is no significant difference between the cases as regard point of onset pain and ultimate pathology, since the cases all start as acute appendicitis.

TABLE VIII  
ONSET PAIN

POSITION OF ONSET	ACUTE	GANGRENOUS	ABSCESSSED	PERFORATED	TOTAL
Epigastric	165	39	25	43	272
Generalized	104	35	15	25	179
Right side	30	2	2	3	37
Left side	0	0	0	1	1
Right lower quadrant	244	34	8	19	305
Right upper quadrant	5	1	2	0	8
Left lower quadrant	2	2	0	3	7
Umbilical	56	18	4	8	86
Upper abdominal	9	5	3	1	18
Lower abdominal	39	15	8	14	76
Not given	16	0	1	4	21
Total	670	151	68	121	1,010

The largest number of patients, about 30 per cent, gave the point of onset pain as the right lower quadrant. About 27 per cent gave the classical epigastric pain and 18 per cent stated the original pain was generalized, with only about 8.5 per cent periumbilical.

The sequence of pain-vomiting is pathognomonic of acute appendicitis, but vomiting is by no means constant. In the simple acute cases only 47 per cent had nausea and vomiting. An additional 33 per cent had nausea without vomiting. It is significant, however, that with increasing severity of the pathology present there was an increasing number of patients who had vomiting as a symptom, increasing to 72 per cent in cases of local peritonitis and 80 per cent in cases of diffuse peritonitis; 54.1 per cent of the entire series vomited.

Fever is a variable sign. It may be stated that a high fever usually indicates a serious condition, but the converse is by no means true. Average temperatures would seem, from this study, significant and roughly an index to the pathology, since the average in simple acute cases was 99°; whereas, with gangrene the average was 99.44° and rose in abscess and peritonitis cases to above 100.5°; the large range between the highest and lowest temperatures given for various types, a range of almost 8° for the series, shows the variability of this sign.

Leucocytosis is also variable and a treacherous sign at times because of the unwarranted reliance placed in it by some men. Here again the averages in this series are typical, showing an increasingly high count with increasing pathology, the average ranging from 12,057 leucocytes in the simple acute cases to 17,728 in the cases of diffuse peritonitis. Here again, however, the range is so great in cases with comparable pathology that one is forced to conclude that it is of value only as one of a number of signs and symptoms and it must be disregarded when at variance with the rest of the picture. Attention must be called to the fact that often a low count in the presence of grave clinical symptoms is a danger signal and regarding it as anything else is likely to lead to disastrous results.

Many consider the differential count of especial significance as an indication of the severity of the infectious process. Without doubt it may be said that it is less often misleading than the total count, but when occasional patients are seen with definite gangrene of the appendix and a polymorphonuclear percentage of 48 or a perforated case with 55 per cent polymorphonuclears it is evident that the differential is not "fool proof" either. On the average, however, the percentage of polymorphonuclears will increase dependent on the severity of the process; this was borne out in our average figures.

In the experience of this clinic by far the most dependable symptom as to degree of infection is the severity of pain, and the most reliable sign is tenderness over the appendix. Usually tenderness will be found in the right lower quadrant in the vicinity of McBurney's point, but occasionally, in a low-lying or retrocecal appendix, tenderness is best demonstrated on rectal examination, because the palpating finger here comes in closest proximity to the involved organ.

#### MORTALITY

It is difficult to comprehend that in spite of new diagnostic aids, in spite of better trained surgeons, in spite of more meticulous technique and increased accessibility of hospitals, the mortality in appendicitis has been increasing for thirty years; but such is the case. Vital statistics, carefully compiled by the census bureau and life insurance companies, have shown a small but progressive rise in the mortality from appendicitis year by year. This is the fact that makes any critical analysis of cases worth while; this is the fact that stands as a challenge to each present-day surgeon; this is, as Royster has so aptly dubbed it, "the tragedy of appendicitis."

An honest effort has been made in this study to determine the pathologic condition present and responsible for the deaths which occurred. This mortality study is not made to flatter the "ego" of this clinic group, although the figures are comparatively good, but to point out the types of cases in which the deaths are occurring as a stimulus to more thoughtful care of these patients.

In the five-year period analyzed, 1,010 cases were diagnosed as acute appendicitis, simple or complicated. With few exceptions this diagnosis was checked by operation or necropsy. In this series there were 21 deaths, a gross mortality of 2.08 per cent. That this figure means little has been stressed, therefore it will be "broken down." There were 670 simple acute cases and 151 gangrenous cases. This gives a total of 821 cases in which the process was limited to the appendix per se; in this group there were 3 deaths, or a mortality of 0.365 per cent. The remaining 189 cases include the perforated ones with local peritonitis, general peritonitis, or a walled-off appendiceal abscess. Where the pathology had extended beyond the confines of the appen-

dix, there were 18 deaths, a mortality of 9.52 per cent. A further analysis of mortality as to pathologic process present is presented in Table IX.

TABLE IX  
MORTALITY IN RELATION TO PATHOLOGY PRESENT

TYPE OF CASE	TOTAL NUMBER	NUMBER OF DEATHS	MORTALITY IN PER CENT
Acute	670	1	.15
Gangrenous	151	2	1.32
Abscessed	68	5	7.14
Perforated with local peritonitis	111	7	6.30
Perforated with diffuse peritonitis	10	6	60.00
Series	1,010	21	2.08

The one death in the simple acute cases was in an obese girl, 17 years of age, with Fröhlich's syndrome who developed bronchopneumonia and peritonitis postoperatively. Both gangrenous cases developed postoperative intestinal obstruction, one having also a pelvic abscess. Of the patients with appendiceal abscesses, 3 died following drainage of the abscess, 1 died of peritonitis following the secondary appendectomy, and 1 died without operation. Of the 7 deaths in the patients with local peritonitis, 4 progressed to diffuse peritonitis postoperatively and 1 died without operation. The 6 deaths in the diffuse peritonitis group are self-explanatory.

It is of interest to compare these figures with other statistics reported in the literature. It is impossible to tabulate all of this information in comparative form because of the varying classifications used, therefore several reported series will be discussed briefly.

Baneroft recently reported a group of 350 cases from the Fifth Avenue Hospital, New York City. There were 15 deaths. There were no deaths in 129 cases showing no adjacent peritoneal reaction; 5 deaths, or 3.3 per cent mortality, in 148 cases with free fluid; a mortality of 4.3 per cent in 46 cases of abscess; and 100 per cent mortality in 8 cases of diffuse peritonitis.

Christopher and Jennings reported, in 1932, a group of 1,138 cases from Evanston Hospital with 47 deaths. Mortality in 955 nonperforated cases was 1.78 per cent; in 183 perforated cases, it was 16.39 per cent.

In 1934 Keyes reported a series from Barnes Hospital, St. Louis. The mortality in 246 simple acute cases was 2.44 per cent; in 193 abscessed cases, 6.22 per cent; and in 56 ruptured cases with peritonitis, 19.64 per cent.

Schullinger reported an eighteen-year group, 1916-1933, at Presbyterian Hospital, New York City. His mortality in simple acute cases was 0.59 per cent in 1,175 cases. In 630 cases with no gross perfora-

tion, but fibrin on the appendix and some peritoneal exudate, probably comparable to our gangrenous group, the mortality was 1.9 per cent. Mortality in 571 abscesses was 10.5 per cent. In 329 cases of diffusing peritonitis the death rate was 17.02 per cent, while in 25 cases of generalized peritonitis it was 88 per cent.

Recently, King of Binghamton, N. Y., reported 364 acute cases comprising those operated in the years 1929 to 1930 and 1934 to 1935. In 248 uncomplicated cases there was but 1 death, or a mortality of 0.4 per cent. Cases of acute local peritonitis carried a mortality of 7.5 per cent; the 32 appendiceal abscesses, 12.5 per cent; and for 17 cases of diffuse peritonitis, 52.9 per cent. The group mortality in the complicated series was 15.5 per cent.

Among the series reported very recently is one by Totten, from the University of Southern California; one by McClure and Altemeier, from Ford Hospital, Detroit; and one by Kirtley and Daniel, of Vanderbilt University, Nashville, Tenn. The California series had a mortality of 4.2 per cent for 7,651 acute cases. The mortality in 6,607 non-perforated cases was 0.78 per cent and for a group of 1,251 perforated cases from July, 1921, to July, 1935, was 23.5 per cent. Ford Hospital reported a total percentage of 10.4 deaths in 252 perforated cases. This included 55 cases of local peritonitis with no deaths; 115 appendiceal abscesses, of which 4.2 per cent died; and 65 cases of general peritonitis and 15 cases of general peritonitis plus abscess, with mortalities of 21.5 per cent and 46.6 per cent respectively. Kirtley and Daniel reported 308 operated cases of perforated appendicitis with a mortality of 16.3 per cent; 4.2 per cent in 118 cases of appendiceal abscess, 8.1 per cent in 87 cases of local peritonitis, and 36.9 per cent in 103 cases of spreading or generalized peritonitis.

It is evident from only a glance at these figures that they are not entirely comparable. It is clear that since the percentages of diffuse peritonitis cases and local peritonitis cases vary so in respect to the total of perforated appendices varying criteria are being used for classification. There are only two comparable figures common to most of these series and these are the total mortalities for the acute cases and the mortalities for the perforated appendices including abscesses, local and general peritonitis. These figures are presented in Table X.

#### TREATMENT

It has been the practice in this clinic to operate upon all cases diagnosed as acute appendicitis nonperforated or upon those in which perforation is thought to have occurred recently, as emergencies. This is without doubt in many cases an unnecessary precaution, but certainly, in a large group of cases, it saves many from passing into the complicated group fraught with a much higher mortality. For a

TABLE X  
COMPARATIVE MORTALITY

SERIES OF:	TOTAL	MORTALITY	TOTAL	MORTALITY
	ACUTE CASES	PER CENT	PERFORATED CASES	PER CENT
Bancroft	350	4.2		
Schullinger	2,730	5.7	925	15.2
King	364	5.2	116	15.5
Christopher-Jennings	1,138	4.13	183	16.39
Totten	7,651	4.2	1,251	23.5
McClure and Altemeier			252	10.4
Kirtley and Daniel	994	5.14	308	16.3
Authors' series	1,010	2.08	189	9.52

number of years, Dr. Donald Guthrie, chief of our clinic, has been a staunch advocate of the Ochsner conservative treatment of those patients who have had perforations several days before being seen and who show a high fever, fast pulse, and abdominal distention. It is in these cases of developing or diffusing peritonitis that we feel the patient is given his best chance by means of Waugensteen drainage, Fowler's position, heat or ice to the abdomen, adequate intravenous chlorides, and physiologic rest of the intestinal tract by frequent administration of morphia. Beekman has pointed out the fact that in infants radical treatment is indicated despite diffusing peritonitis because of the inability of the small child's omentum and abdominal viscera to wall-off infection. In cases which have begun to localize an abscess when first seen, there can be little doubt of the treatment to be followed. These patients are treated conservatively until the temperature and pulse have receded and localization is complete. At this point they are drained and the appendix removed only if accessible. If the organ is not removed, the patient is strongly advised to return for secondary operation in six weeks to two months.

It is of interest in this connection that, of the 67 cases of appendiceal abscess operated upon in this series, it was deemed wise to remove the appendix in only 15, or 22 per cent. of the cases. Of the remaining 52 patients, 38 subsequently returned for secondary appendectomy. Of the 15 patients from whom the appendix was not removed primarily or secondarily in this clinic, it seems likely that a good proportion have subsequently been induced or forced by further infection to have it removed at some other institution.

The surgeons of the Guthrie Clinic have been slow to abandon the operation of enterostomy in complications of appendicitis because of the belief founded on experience that it still saves lives in certain cases doomed in spite of the yeoman's service rendered in many cases by Waugensteen decompression. That it is not necessary to resort to it so often as previously is not only admitted but attested to. In this series enterostomy was resorted to in 10 cases, or practically 1 per

cent of the series. This was complementary at the time of original operation in 6 cases and secondary, three to six days postoperative, in 4 cases. That the operation was of value is evident when we consider that 50 per cent of these distended, critically ill patients recovered.

TABLE XI  
ENTEROSTOMIES

TYPE CASE	COMPLEMENTARY	SECONDARY	NUMBER DIED	PER CENT DIED
Gangrenous	0	2	2	100
Abscessed	3	0	2	66
Perforated	3	2	1	20
Total	6	4	5	50

*Drainage.*—In recent years the old dictum “when in doubt, drain” has become “when in doubt, don’t drain.” In accord with this trend we have found in the more recent cases of this series a decreasing number of drained cases, especially in the gangrenous cases and early perforations.

TABLE XII  
DRAINAGE

TYPE OF CASE	TOTAL NUMBER	NUMBER DRAINED	PER CENT DRAINED
Acute	670	9	1.3
Gangrenous	151	37	24.7
Abscessed	68	69	100.0
Perforated with local peritonitis	111	81	73.0
Perforated with general peritonitis	10	3	30.0
Total	1,010	100	19.7

(2 operated upon twice; 1 not operated upon)

It will be seen by Table XII that less than 20 per cent of all the cases were drained; 73 per cent of the perforated cases were drained and about 25 per cent of the gangrenous cases.

*Associated Conditions and Complications.*—A number of associated conditions were present in cases of this series. Many were incidental conditions which bore no relationship to the primary condition and influenced it little. A few will be mentioned which may be of significance. Acute tonsillar infection was present in 5 cases. Some have felt coexisting tonsillar infection to be significant in etiology; its infrequency in this series proves nothing. Six patients in the series were diabetics. No deaths occurred in these cases, proving the safety with which acute surgery may be done in diabetics when carefully managed. Pregnancy was present in 3 acute cases which were operated upon without mortality to fetus or mother. Three of the patients were



tuberculous and 10 of the female patients had coexisting salpingitis. Two had Meckel's diverticula, asymptomatic and discovered accidentally.

The more important and frequently occurring complications are summarized in Table XIII.

TABLE XIII  
COMPLICATIONS IN RELATION TO PATHOLOGY PRESENT

COMPLICATION	ACUTE	GANGRE- NOUS	AB- SCESSED	LOCAL PERI- TONITIS	DIFFUSE PERI- TONITIS	TOTAL
Postoperative peritonitis	1	1	3	5		10
Postoperative intestinal obstruction	0	3	0	2	0	5
Pelvic abscess	2	0	4	3	1	10
Pneumonia	1	1	0	1	1	4
Atelectasis	1	0	0	0	0	1
Pulmonary embolus	0	2	0	2	0	4
Wound abscess	3	5	1	2	0	11
Hemorrhage	2	0	1	0	0	3

Spreading peritonitis postoperatively accounted for most of the post-operative deaths in the local peritonitis groups and in the appendiceal abscesses as well as the one simple acute case which ended fatally and one of the gangrenous. The incidence of other complications is also of interest. Intestinal obstruction occurred in 5 patients and 10 had pelvic abscesses. Pulmonary complications were infrequent and only 4 cases of embolus with 1 death occurred. Eleven wound abscesses occurred.

#### SUMMARY

A series is presented of 1,010 consecutive cases of acute appendicitis seen on the surgical service of the Guthrie Clinic and Robert Packer Hospital during the five years from June 1, 1932, to May 31, 1937. During this period there were 21 deaths, including nonoperated as well as operated cases. This gave a group mortality of 2.08 per cent for acute appendicitis in this clinic. Eighteen of these deaths were in the 189 cases in which the appendix had grossly perforated, a mortality for this group of 9.52 per cent. The mortality in the 10 cases carefully selected which had general peritonitis on admission was 60 per cent. These figures were compared with some other series recently reported in the literature.

As an aid to diagnosis, certain predisposing factors, age, sex, and seasonal incidence, were analyzed as well as the relationship of cathartic intake and postponement of treatment to development of complications and mortality. Certain symptoms and signs, including the incidence of nausea and vomiting, position of onset of pain, febrile reaction, leucocytosis, and differential count, were analyzed and although

average findings were found to be typical in each type of pathology the variability was found to be great.

Treatment was discussed, stressing the value of early operation in the nonperforated cases and early perforated cases but the advantages of delayed operation in late perforated and diffuse peritonitis groups, as well as in cases of localized appendiceal abscess. Drainage of cases and enterostomy as a complementary and secondary procedure in selected cases were analyzed. It may be stated here in relation to treatment that almost without exception the McBurney incision was used as operative approach in these cases.

Finally, associated conditions and the complications occurring post-operatively were listed and discussed.

#### CONCLUSIONS

1. The age group in which appendicitis most frequently occurs is in the five-year period from 16 to 20 years of age. It may occur, however, at any age and the incidence of complications, i.e., gangrene and perforation, is higher proportionately in the ages before 6 and after 50 years.

2. The male is more frequently afflicted and is more likely to have the infection go on to complication than the female.

3. Some seasonal variation in the incidence of appendicitis exists. The incidence is about 15 per cent greater in the spring and summer months than in the fall and winter months.

4. The principal predisposing factors to complications of acute appendicitis are the administration of laxatives and delay time between onset of disease and surgical treatment.

5. The symptoms and signs of appendicitis, although following average trends in relation to the severity of the pathology present, vary markedly in cases with the same pathology present. We believe tenderness over the appendix to be the most reliable sign.

6. Mortality of this series was analyzed and found to compare favorably with other series recently reported.

7. We believe our favorable mortality to be due to early emergency treatment of all early cases of acute appendicitis with conservative treatment of localizing abscesses and certain severely ill late cases of perforation with local or diffuse peritonitis. We believe the use of the McBurney incision is of value in lowering mortality because of the accessibility of the appendix and diminished trauma to bowel and unlikelihood of spreading infection when perforation has already occurred. The close coordination in this clinic between the intern, fellow, and full-time senior staffs in carrying out preoperative, operative, and postoperative treatment has certainly been a factor in maintaining a favorable mortality rate.

8. The use of drainage material is decreasing on our service although drainage is still used in many cases of perforation and, of course, in treatment of appendiceal abscess. Drainage is being used infrequently in gangrenous nonperforated cases even when cloudy fluid is present.

9. Enterostomy is still a useful operation in some badly distended patients who do not respond to Waagensteen deflation.

10. Diffuse peritonitis is the usual cause of death in acute appendicitis.

11. An appeal is made to other groups to analyze their cases in respect to the pathology present, since group mortality figures mean little and it is only by such a "break-down" analysis that one can arrive at any conclusions as to the value of any method of treatment in the cases which have progressed to perforation with its attendant high mortality.

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# NONDRAINAGE IN COMPLICATED APPENDICITIS

## REVIEW OF 109 CONSECUTIVE CASES

FRANK W. PICKELL, M.D., BREWTON, ALA.

A GENERAL review of the literature has convinced me that no dogmatic statement on the question of drainage in appendicitis can be made by a study of the literature. The old dictum, "If you are in doubt, drain," seems more and more in the past few years to be replaced in the minds of some surgeons by the contrary principle: "If in doubt, don't drain." Having this in mind, I wish to contribute my results with nondrainage operative treatment in a consecutive group of 109 cases of appendicitis complicated with peritonitis or rupture. I hope that in the future many such contributions may crystallize a uniform opinion on this controversial subject.

### MORTALITY OF APPENDICITIS

The average mortality for appendicitis of all kinds from American and European clinics is about 5 per cent.<sup>1</sup> It is well known to all surgeons that the so-called "clean" cases of acute appendicitis have a negligible mortality, but the more serious cases, or the old so-called "drainage group" where the pathology no longer remains within the peritoneal coat of the appendix,<sup>2</sup> according to most writers on the subject, carry a mortality of from 10 to 25 per cent or more, excluding the cases of localized abscess.

Guthrie<sup>2</sup> in an editorial says our attention should be only on those cases of appendicitis in which the pathology no longer remains within the appendix and terms those cases "appendicitis with complications." He ventures the opinion that the conservative measures of treatment should show a far lower mortality, but he does not state exactly what he considers the conservative measures to be.

Kehl and Rentschler<sup>3</sup> in their series of 126 such serious cases had a mortality of 12.6 per cent. They practically routinely used drainage.

Haggard<sup>4</sup> in 379 cases of ruptured appendices reports a mortality of 5 per cent and in 186 cases of generalized spreading peritonitis with gangrenous perforation, 24.7 per cent. In 1,650 less acute cases his mortality was 0.72 per cent. He quotes other authors with somewhat the same figures on mortality.

### NONDRAINAGE TREATMENT AND MORTALITY

Spivaek<sup>5</sup> states that some surgeons, notably, Carl A. Meyer, of Chicago, in gangrenous appendicitis or if free pus and fluid have been

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8. The use of drainage material is decreasing on our service although drainage is still used in many cases of perforation and, of course, in treatment of appendiceal abscess. Drainage is being used infrequently in gangrenous nonperforated cases even when cloudy fluid is present.

9. Enterostomy is still a useful operation in some badly distended patients who do not respond to Wangensteen deflation.

10. Diffuse peritonitis is the usual cause of death in acute appendicitis.

11. An appeal is made to other groups to analyze their cases in respect to the pathology present, since group mortality figures mean little and it is only by such a "break-down" analysis that one can arrive at any conclusions as to the value of any method of treatment in the cases which have progressed to perforation with its attendant high mortality.

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"A foreign body, such as a drain, has been shown to lower the natural immunity of the peritoneum against infection. (This would indicate that drainage is a menace rather than a help.)

"Drainage causes temporary loss of the normal defensive peritoneal fluid.

"There is a longer and more stormy convalescence because of the added pathologic changes caused by the foreign body, resulting in partial obstruction, ileus and increased peritonitis.

"An intra-abdominal drain through an infected wound attracts and harbors all the dependent suppuration of that wound. The profuse purulent discharge from such a drained wound arises primarily from suppuration in the wall and not from within the cavity. The depth of such a drainage tract therefore collects suppuration from the abdominal wound, and hence the intra-abdominal infection surrounding the drain is aggravated.

"There is a high incidence of early and late postoperative herniae.

"Necrosis from the pressure of the drain has been the cause of many fecal fistulas and fatal hemorrhages. (There was only one fecal fistula in the 1,000 cases, a case in which drainage was employed.)

"Drainage has increased the incidence of secondary intra-abdominal abscesses in the series."

#### REVIEW OF CASES

Tabulated as Table I are 109 consecutive cases presented by myself. These cases have been operated upon in the past 4½ years of practice. They are all of my cases in which at operation local or generalized peritonitis was found present. No cases of this classification were excluded. Excluded from this series were all "interim appendices" or appendices removed while doing some other operation, all localized appendiceal abscesses drained, and all acute appendices in which the inflammation was confined within the appendix. Three-fourths of these 109 cases were found in the age group between 15 and 40 years. There were 49 males and 65 females.

The cases are divided into three main groups. In the first group are those cases in which at operation a local peritonitis about the appendix was present as evidenced by acute inflammation of the appendix and fresh adhesions of omentum or small gut to the appendix. The appendix in such cases was partially or totally gangrenous with pus around it. This group comprises 70 cases, obviously the cases that came to operation earliest. The mortality in this group was 0. None of these cases were drained though many times at operation doctors assisting or looking on advised drainage. Only 12.9 per cent of these cases had taken purgatives.

The second group of cases totaled 30 and were those with spreading or generalized peritonitis and the appendix was invariably totally

found in the abdominal cavity, close the peritoneum by suture and then drain the rest of the anterior abdominal wall or close it completely, depending on the gravity of the infection. Their opinion is that the peritoneum will take care of the infection and if it cannot take care of it itself no drains will save the patient.

Thorek<sup>6</sup> states that at the Cook County Hospital in Chicago some surgeons of the staff often omit drainage and obtain excellent results.

Willis and Mora<sup>7</sup> in a study of 100 ruptured or acute suppurative cases of appendicitis with only one fatality and a study of the literature conclude: "Drainage after operation for ruptured or gangrenous appendicitis does not subtract from the mortality but does add to the morbidity." Their own study of 100 cases demonstrates the comparative safety of closing the abdomen without drainage following operation for acute suppurative appendicitis.

Potter<sup>8</sup> believes a lower mortality in acute diffuse peritonitis following acute appendicitis is favored by employment of suitable means to prevent ileus, for which he recommends pitressin; but he also emphasizes early operation with removal of the appendix, minimal drainage of the peritoneal cavity, and adequate amounts of water, salt, and glucose to supply fluid and chemical deficiencies.

In the *1936 Yearbook of General Surgery*<sup>9</sup> it is stated that at Utrecht in Holland the less frequent use of drainage in acute appendicitis does not appear to have had unfavorable influence on mortality and on the other hand has shortened the postoperative hospital stay. But, it is also stated that the decreased mortality is due to earlier operation.

In the *1937 Yearbook of General Surgery*<sup>10</sup> Cafritz advises nondrainage in appendiceal peritonitis and presents twenty-five cases in which nondrainage was successfully carried out.

Rhodes<sup>1</sup> in reviewing 1,000 consecutive cases of acute appendicitis at a San Francisco Hospital gives figures showing decidedly less mortality in cases nondrained as compared with those drained. In 32 cases of gangrenous unperforated appendicitis that were drained, the mortality was 9 per cent and in 224 later cases of the same kind not drained the mortality was 0.9 per cent. In 89 gangrenous perforated cases that were drained the mortality was 10 per cent, while in 113 later cases of the same kind that were not drained the mortality was only 2.4 per cent. They state that for several years they have averted all intra-abdominal cases drained in peritonitis. Perforated ulcers, traumatic injuries of the gastrointestinal and genitourinary tracts are closed without drains. It is only in the chronic, well walled-off abscesses that they still use drains. They state the case against drainage in peritonitis as follows:

"Within a few hours the drain ceases to act other than as a foreign body which is walled off by adhesions.

I do not believe in the delayed treatment, especially in rural or small town practice. In all of the cases but one the appendix was removed. The abdomen was opened by a right rectus or right paramedian incision. I believe in long incisions especially in these types of appendices as they are often misplaced and are hard to find unless there is adequate exposure. Thorough abdominal exploration is impossible through a McBurney incision and any enlargements of it will injure the abdominal wall greatly. McBurney himself did not advise its use in acute cases.

The only departures from usual operative procedures in these cases were as follows:

1. First was the method of locating the appendix after the abdominal cavity was opened. The operator stood on the left side of the patient and had the assistant strongly retract the right rectus muscle with its underlying fascia and peritoneum laterally and slightly anteriorly. While the assistant did this, the operator pushed in a moist abdominal pack on top of the omentum and intestines and with this "crawled" over the intestines and omentum to the ileocecal region where he located the appendix by direct vision. In introducing this pack and "crawling" over it to the region of the appendix and then leaving it in situ until after the appendix was removed, further contamination of the abdominal cavity was averted more completely than in any other method that I have ever tried or found in the literature. This pack caught all spill or contamination. It was not removed until all operative manipulation around the appendix was over and all mopping out or suction was completed.

2. Ligation of the appendix was practiced and none in this entire series was purse-stringed or inverted. This was time saving and was never regretted. In nearly every case the ligated mesoappendix was tied to the ecarbolized stump of the appendix.

3. No drainage was used, with the exception of four earlier cases.

#### PRE- AND POSTOPERATIVE CARE

As all cases were operated upon at once after the diagnosis was made, there is little to say about preoperative care. Postoperatively, all cases were given water, salt, and glucose by hypodermoclysis or infusion and all food and liquids by mouth were withheld until it was believed the peritoneum had eared for the infection and normal peristalsis could safely be restarted. This period varied from two to ten days. Morphine was given until it was felt safe to resume peristalsis, but never less than three days. Postoperative care was as great a factor in the successful management of these cases as the operation.

#### COMMENTS

1. This series of cases shows the safety of closing the peritoneal cavity without drainage.



TABLE I

109 CONSECUTIVE APPENDECTOMIES IN ACUTE APPENDICITIS CASES THAT WERE COMPLICATED WITH LOCAL OR GENERALIZED PERITONITIS

	ACUTE, PARTIALLY OR TOTALLY GANGRENOUS WITH LOCAL PERITONITIS	ACUTE GANGRENOUS WITH SPREADING OR GENERALIZED PERITONITIS	ACUTE RUPTURED CASES, PARTIALLY OR TOTALLY GANGRENOUS BEFORE RUPTURE	TOTAL
No. of cases	70	30	9	109
Deaths	0	3	1	4
Percentage of deaths	0	10%	11.1%	3.7%
Percentage that took purgative after onset of acute symptoms	12.9%	63.3%	100%	34.1%
Drained	0	1	3	4
Died that were drained	0	0	0	0
Saved by drain	0	0	1 ?	1
Died that might have been saved by drain	0	1 ?	0	1
Cases having acute intestinal obstruction on sixth day or later with operation for	1	1	0	2

gangrenous. There was a large amount of fluid or pus widespread in the abdominal cavity and large areas of the peritoneum were inflamed even as distant as the upper abdomen or pelvis. Of these cases 63.3 per cent had taken purgatives and 3, or 10 per cent, died. One case was drained and one possibly could have been saved by drainage, though I think not. All of this second group would have been drained by any surgeon believing in the efficacy of drainage at all.

Comprising the third group were 9 cases in each of which rupture had occurred before time of operation; feces or infected contents of the ruptured appendix were being poured out into the abdominal cavity. One of these patients died, giving a mortality of 11.1 per cent for this group. Three of the earlier cases in this group were drained. None of the cases drained died and one of the drained cases was considered as possibly being saved by the drain, although I do not subscribe to this view. Nine of these cases of ruptured appendix took purgatives after the onset of the acute appendicitis. The mortality for the 37 cases that took a purgative after onset of symptoms of acute appendicitis was 10.9 per cent. The combined mortality for these 109 cases was 3.7 per cent.

#### OPERATING METHODS USED

All of these cases, as well as all cases of appendicitis, were operated upon at once when the diagnosis of appendicitis was made.

## INTERNAL BILIARY FISTULAS

A DISCUSSION OF INTERNAL BILIARY FISTULAS BASED ON 29 CASES  
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APPROXIMATELY 1.2 per cent of all the patients with cholecystitis admitted to the University Hospitals since 1915 have had internal biliary fistulas. Such a complication should be suspected in every patient suffering from a long-standing biliary tract disease. In a series of 10,866 routine necropsies Roth, Schroeder, and Schloth<sup>2</sup> found 43 biliary fistulas.

Table I includes practically all types of internal biliary fistulas that have been reported in the medical literature.

TABLE I

- 
- |  |
|--|
| 1. Duodenal  |
| a. Cholecystoduodenal  |
| b. Choledochoduodenal  |
| c. From cystic duct to duodenum  |
| d. From reformed gall bladder (dilated stump of cystic duct) to duodenum |
| 2. Colic, cholecystocolic  |
| 3. Gastric   |
| a. Cholecystogastric   |
| b. Choledochogastric   |
| 4. Jejunal, cholecystojejunal  |
| 5. Mixed, from biliary tract to two or more viscera                      |
| 6. Bronchial   |
| a. Cholecystobronchial   |
| b. Choledochobronchial   |
| c. Hepatobronchial   |
| 7. From biliary tract to kidney pelvis or ureter                         |
| 8. From biliary tract to urinary bladder                                 |
| 9. From biliary tract to uterus or vagina                                |
| 10. From biliary tract to pleura   |
| 11. Between the bile ducts   |
| 12. From biliary tract to portal vein                                    |
| 13. From biliary tract to hepatic artery                                 |
| 14. From biliary tract to pericardium                                    |
| 15. From biliary tract to an ovarian cyst                                |
- 

The varieties listed under Types 1 to 6 are given in the order of their relative frequency and importance. Bronchobiliary fistulas are rather uncommon in the United States, but they assume greater importance in the tropical countries where liver abscesses are developed more frequently. Divisions 7 through 15 include rare and relatively unimportant types of fistulas. It is, however, entertaining and somewhat startling for even the medical man to learn that gallstones have been found plugging the portal vein or hepatic artery, that both men

2. Postoperative care played a large part in the recovery of all of these cases.

3. The danger of taking purgatives in acute appendicitis is clearly demonstrated by these cases, which show that 100 per cent of the ruptured and 63.3 per cent of those with spreading or generalized peritonitis had been thoroughly purged after the onset of their acute appendicitis. The mortality of these "purged" cases was 10.9 per cent.

4. Complications in this series were relatively infrequent considering the seriousness of each case and were not aggravated by lack of drainage.

5. The method of introducing an abdominal pack and "crawling" over it to the appendiceal region aided in preventing further spread of the spill from the infected focus of the appendix during both exploration and removal of the appendix.

6. A detailed study of the fatal cases found no basis for the belief that drainage or delayed operation would have saved any of them.

7. A consideration of the four drained cases showed the futility of drainage.

#### RESULTS

Using nondrainage treatment in all but 4 early cases in a series of 109 consecutive appendectomies complicated by local or generalized peritonitis, a mortality of 3.7 per cent was encountered. These figures compare favorably with most reports in the literature.

#### CONCLUSION

Nondrainage treatment of peritonitis from gangrenous or ruptured appendicitis can be concluded as safe and as a factor in reducing both mortality and morbidity.

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## SYMPTOMS, SIGNS, AND DIAGNOSIS

The average history in this series revealed repeated attacks of biliary tract disease. The longer the trouble had persisted, the more likelihood of there being a fistula present. One patient complained of recurring episodes for 30 years, and several had attacks for over 20 years. The average duration of the biliary tract complaints was 12 years.

The symptoms, which often included colic, fever, dull pain, dyspepsia, nausea, vomiting, intolerance to fatty foods, constipation, diarrhea, or jaundice, were essentially those associated with nonfistulous biliary tract disease. Fever, which is supposedly more marked with fistulas, was an inconstant finding. If any variation is noted, it is that with fistulas the attacks were usually more severe and gradually increased in duration and intensity. The patients frequently suffered the most severe and prolonged attack just before entering the hospital.

The textbooks on biliary tract diseases<sup>5-7</sup> indicate that many patients receive sudden, prolonged, or even permanent relief from all symptoms when the fistulas are formed and the septic biliary contents are liberated into the gastrointestinal tract. Only one patient in this series reported temporary relief when the fistula was formed, but she developed an acute intestinal obstruction due to gallstones within forty-eight hours. No history of prolonged or permanent relief was found.

The vomiting of gallstones is supposedly pathognomonic of the formation of a fistula between the biliary tract and the stomach. It is also said that pus and blood in the vomitus may indicate the formation of a fistula to either stomach or duodenum. The colic type of fistula is thought to produce diarrhea or to cause peculiarly colored stools which contain unevenly mixed and unoxidized bile. None of the above findings, however, were elicited in this series.

Intestinal obstruction due to gallstones that have passed through fistulas is reported in the textbooks<sup>5-7</sup> and literature<sup>1, 13</sup> as a rare secondary complication. In this series, however, 9 cases of intestinal obstruction were discovered. The calculi were impacted somewhere along the small bowel in 7 cases, and in 2 cases the obstruction was due to inflammatory adhesions about the fistulas which contained calculi. The diagnosis of acute intestinal obstruction due to gallstones should be considered in any patient who suddenly develops obstructive signs and symptoms after a prolonged siege of biliary tract disease.

The passage of gallstones with the feces is always suggestive of an internal biliary fistula, but the stones are definitely significant only if they are too large to have passed through the ampulla of Vater. One of three patients who were diagnosed preoperatively in this series passed small gallstones rectally on several occasions, but during one defecation she passed such a large calculus that she fainted during its painful delivery.

and women have passed gallstones in the urine, that biliary calculi have been found with the placental membranes following labor, or that the pleural and pericardial sacs have been invaded and forced to retain the contents of a diseased gall bladder. If space permitted, a discussion of the pathogenesis<sup>11, 12</sup> of only these rarer forms would give one a better understanding of the other varieties.

This study is based on 29 cases from the University Hospitals. It includes 24 cholecystoduodenal fistulas; 1 cholecystogastric; 1 choledochoduodenal; 1 cholecystocolic; 1 fistula from a hepatic duct to the duodenum; and 1 from a reformed gall bladder to the duodenum. The latter 2 fistulas are apparently unique since no other similar cases were encountered in the literature. Twenty-seven of the patients were females. The average age for the group was 58 years, the youngest being 25 and the oldest 83 years.

Cholecystoduodenal fistulas are the most common type. Nannyn<sup>3</sup> reported 193 cases of which 93 connected the gall bladder and duodenum, 49 led to the colon, and 15 led to the lower end of the stomach. Judd and Burden<sup>1</sup> collected 153 cases of which 117 were duodenal, 26 were colic, and 6 were gastric. Nannyn<sup>3</sup> also reported 15 cases of choledochoduodenal fistulas and 2 cholecystojejunal fistulas. Fistulas between the common duct and duodenum are probably more common than is generally supposed.

#### PATHOGENESIS

Except for those fistulas established surgically for the purpose of obviating persistent biliary obstruction, all internal biliary fistulas are of spontaneous origin. Often the pathogenesis is as follows: After repeated attacks of acute inflammation, the gall bladder or bile ducts become adherent to the nearest portion of gut. The first part of the duodenum, the proximal end of the transverse colon, and the pyloric end of the stomach are the usual sites of involvement in order of their frequency. Then during an acute attack perforation of the adherent visceral walls occurs due to the necrotizing action of contained calculi or bulging empyema. The fistulous tract is then established, and the septic contents of the biliary tract are liberated into and carried away by the gastrointestinal tract. Another possibility is that rupture of a diseased gall bladder produces a pericholecystic abscess which secondarily necrotizes the gut wall to establish the fistula.

In all probability stones are essential in the formation of all spontaneous internal biliary fistulas except the more uncommon cases due to carcinoma in the biliary tract or to perforating peptic ulcers. Fifteen cases in this series were proved to have cholecystolithiasis; 10 had stones in the common duct; and 3 had bile sand in the common duct. Stones were found in transit in 2 fistulas.

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The second patient diagnosed preoperatively had developed a tender palpable gall bladder during a typical attack of acute cholecystitis. After a few days the palpable mass disappeared together with the associated acute pain. Within the next forty-eight hours the patient developed an acute intestinal obstruction and at operation a large gallstone was found impacted in the lower ileum. This patient is also the only one in whom the symptoms indicate the time of formation of the fistula.

The third case diagnosed clinically was the cholecystocolic fistula which was found during a routine roentgenologic examination of the colon. The barium mixture passed through the fistula to fill the gall bladder and biliary radicles which were then easily visible on the roentgenogram. Roentgenologic studies are only rarely of aid in the diagnosis of internal fistulas. One interesting case report by Vorhaus and Rogers<sup>4</sup> describes a cholecystocolic fistula which was accidentally visualized roentgenologically by means of gas which passed from the colon through it to fill the biliary radicles.

The diagnosis of an internal biliary fistula is rarely made during the clinical examination, and the fistula is usually an accidental finding at the operating table. Even then it may be missed, as in two patients who were thought to have carcinomas after large ligneous masses had been found at operation. The post-mortem examinations in both cases, however, revealed the carcinomatous-like masses to be composed of dense cicatricial tissue surrounding fistulous tracts and calculi. Twenty-six of the fistulas in this series were not diagnosed as such until after operation or post-mortem examination.

#### PROPHYLAXIS

What can be done to prevent the formation of internal biliary fistulas? At present the best prophylactic measure is the removal of the gall bladder and all calculi in the early stages of the biliary tract disease. An obstruction in the biliary channels is without doubt a dominant factor in the production and maintenance of a fistula. Relief of this obstruction in most cases would allow the tract to heal spontaneously. Moreover, the tendency for the fistula to be healed or obliterated by cicatricial tissue is so great that it practically never serves any length of time as an adequate channel for the flow of bile and therefore never gives prolonged relief from the biliary tract symptoms. For that reason it is imperative to relieve the biliary tract pathology before the fistula develops.

#### OPERATIVE FINDINGS AND DIFFICULTIES

After the fistula has been established, the difficulties of the operative procedures are greatly increased. The surgeon frequently finds the viscera in the right upper abdomen to be so closely matted by inflam-

matory adhesions that no line of cleavage is discernible, and adequate exposure is obtained only by blind probing and cutting. The walls of the gall bladder and bile ducts are usually thickened and fibrotic from repeated attacks of inflammation. Previous operative procedures merely add to the amount of scarring and fibrosis. Not uncommonly the adhesions in the pericholecystic area are so dense and massive that drainage of the gall bladder is all that dare be attempted.

If the surgeon is to cure the patient, however, he is confronted not only with the necessity of relieving the original biliary obstruction, but in addition he is forced to excise the fistula and then close the defect which remains in the involved portion of gut wall.

Sometimes the fistula is nothing more than a side-to-side anastomosis between the affected viscera. Again it may be several centimeters long running through heavy cicatricial tissue and containing much necrotic and septic debris in its lumen which may be pinhole in size or large enough to allow the passage of a large stone. When the lumen is small, the surgeon may excise the fistula and inadvertently overlook the opening in the gut wall, with the result that peritonitis, subphrenic abscess, pelvic abscess, or even death supervenes. If the fistulous lumen is large, the cavity must often be drained like any other intra-abdominal abscess.

The defect in the gut wall may be surrounded by friable scar tissue which makes the repair very difficult and which makes the possibility of a permanent closure a questionable one. Most of the fistulas lead to the duodenum which is noted for its resistance to successful closure. If the defect is successfully sutured or a purse-string inversion of the ligated fistulous tract is obtained, a stricture of the gut wall may result. A gastroenterostomy or some other shunting operation is then required. The above difficulties are further increased if the fistulas are multiple or enter more than one division of the gastrointestinal tract.

If intestinal obstruction has developed due to calculi, strictures, or hypertrophic mucosa, the entire surgical attack sometimes must be directed toward relieving the bowel obstruction. The fistulous tract is then left intact with the hopeful prayer that the patient will not develop biliary obstruction, suppurative cholangitis, or greater liver damage before the gastrointestinal condition has subsided.

Associated pathologic findings may include acute or chronic hepatitis and pancreatitis. Both of these conditions are undoubtedly present more frequently than recognized, and they greatly increase the patient's as well as the surgeon's difficulties. Liver damage in 3 cases which came to autopsy was reported as acute hepatitis, occlusive biliary cirrhosis, and suppurative cholangitis respectively. Pancreatitis was noted in 10 cases.



Unfortunately the patients in this series did not receive adequate prophylactic care. Although the average duration of symptoms was 12 years, 24 of the 29 cases had had no previous surgical procedures on their biliary systems. Three of the previously operated cases had had cholecystostomies, and only 2 had had cholecystectomies. One of the cholecystectomy cases had a fistula from a hepatic duct to the duodenum and the other had a fistula from a re-formed gall bladder to the duodenum.

#### OPERATIVE PROCEDURES AND RESULTS

Twenty-five of the patients were treated at the University Hospitals by operative procedures which included 12 cholecystectomies, 1 cholecystostomy, 9 choledochostomies, 1 transplantation of the common duct, 12 duodenal repairs, 2 gastric repairs, 3 gastroenterostomies, 4 enterostomies for removal of stones, 1 laparotomy for the crushing of a gallstone in the lower ileum, and other lesser procedures. Two patients died as a result of the fistulas and related complications before surgery could be instituted. Two patients refused surgery. Twelve of the patients receiving surgical treatment were relieved by the operative procedures, although the 1 patient treated by cholecystostomy developed a persistent external biliary fistula. Thirteen of the cases died following the surgical procedures.

#### MORTALITIES

The following brief analysis of the mortalities emphasizes the complications and difficulties that may arise in the treatment of these patients.

Five cases died as a result of intestinal obstruction due to biliary calculi. Two of these expired even before surgery was instituted. A sixth death due to intestinal obstruction resulted from marked scarring and contraction about a cholecystoduodenal fistula and several calculi.

In 3 cases peritonitis following the difficult operative procedures was the main cause of exodus. One of these was complicated by acute hepatitis and nephritis, another had an impacted common duct stone, and the third had bronchopneumonia.

One patient died after many repairs of the common duct and one choledochoduodenal intubation had been carried out. The autopsy revealed suppurative cholangitis, stenosis of the common duct, an external biliary fistula, a fecal fistula from the colon, and an occlusive biliary cirrhosis of the left lobe.

In 3 deaths the causes were varied: first, postoperative shock and septicemia; second, subphrenic abscess; third, partial obstruction of the common duct and bronchopneumonia.

Death in 2 cases was not related to the disease of the biliary tract since the autopsies revealed a carcinoma of the cecum in 1 patient and an infected decubitus ulcer with septicemia in the other.

Due to the fact that these patients present such a myriad of possibilities, individual study of each case is necessary for a thorough explanation of the final outcome. It would seem from this study, however, that delay and lack of prophylactic treatment were essentially responsible for 13 of the deaths, 2 deaths being unrelated to the biliary tract disease. The 3 cases of peritonitis, the subphrenic abscess, and the case of postoperative shock and septicemia were definite sequelae of the surgical procedures. In the remaining 8 deaths, however, the dominant factor is the persistence of untreated biliary tract disease.

#### CONCLUSIONS

1. The formation of a communication between the biliary tract and gut is sometimes a life-saving accident because it allows inflammatory debris and calculi to be spontaneously extruded from the biliary system and to be carried away with the feces.

2. Nevertheless, it breeds possibilities for greater liver damage by providing an open channel through which septic intestinal contents are flushed into the biliary radicles.

3. It rarely provides adequate biliary drainage because scar formation and contracture of the fistulous lumen begin almost as soon as the communication is established. Future biliary obstruction is therefore inevitable unless curative surgery is instituted.

4. It usually occurs after a prolonged history of biliary tract disease which has gradually been increasing in severity and which most likely has never been approached surgically.

5. It fosters the development of various types of intestinal obstruction arising from impacted gallstones, scarring of the gut walls, inflammatory adhesions, or hypertrophic mucosa.

6. It impedes accurate diagnosis and, although its presence should always be suspected in cases of long-standing biliary tract disease, it usually cannot be proved preoperatively.

7. It increases the risk of surgical treatment many times over that of uncomplicated biliary tract disease which has an operative mortality of 1 to 5 per cent.

8. It greatly increases the nonoperative mortality and morbidity of biliary tract disease.

9. The bulk of evidence indicates that practically all internal fistula to the gastrointestinal tract can be prevented by early surgical treatment of the predisposing chronic cholecystitis or related biliary tract disease and that delay should be strenuously avoided.

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## BACTERIAL AGGLUTININ IN BILE OF PATIENTS WITH CHOLELITHIASIS

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THE relation of infection and cholelithiasis has received considerable attention, although a specific mechanism which is responsible for gallstone formation has not yet been described. It has recently been demonstrated that the gall-bladder wall, when damaged by infection, permits bile salts to be rapidly absorbed from the gall-bladder bile<sup>1</sup> and it has also been shown that hepatitis results in a bile in which the bile salt concentration is greatly reduced. A reduction in the bile salt concentration may permit cholesterol to precipitate out of the bile. This mechanism is perhaps an important one in gallstone formation but it is quite possible that other factors also may be involved. I have found that agglutinins appear in the bile of dogs in response to a specific infection.<sup>2, 3</sup> The presence of antibody in bile may be a significant factor in stone formation because of its ability to cause agglutination or precipitation, thus providing a nidus for stone growth. The present study demonstrates that antibody is present in human bile and that the agglutinin content of human bile varies in individuals with disease of the biliary apparatus being greatest in patients with cholelithiasis.

### METHOD

Material for this study was obtained from patients on the surgical services of Dr. I. S. Ravdin and Dr. E. L. Eliason in the Hospital of the University of Pennsylvania. After exposing the gall bladder, its contents were aspirated and the bile was placed in a sterile container. In those patients in whom drainage of the common duct was instituted, samples of hepatic bile were obtained for study. All specimens removed at the operating table, and subsequent to operation, were collected under aseptic precautions. In the majority of cases within forty-eight hours of operation blood from the antecubital vein was obtained for serum agglutinin titer and blood culture.

One-half cubic centimeter of bile was inoculated into glucose-beef and plain beef-infusion broth for study under aerobic and anaerobic conditions. Samples of bile and serum were studied for the presence of agglutinin to *Staphylococcus aureus*, *B. coli*, and *B. typhosus*.

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The agglutination tests were performed by serial arithmetic dilution of the serum and bile to a volume of 0.8 c.c. with isotonic buffered phosphate solution (pH 7.4) which contained 0.014 thymol. Bacterial antigen was added so that the total volume was 1 c.c. The agglutination test tubes were incubated at 37° C. for twenty-four hours and were then examined with a hand lens for evidence of agglutination. Where there was any doubt about agglutination, the test tubes were centrifuged and the sediment was resuspended in 1 c.c. of physiologic saline solution, after which they were examined again for evidence of agglutination. Simultaneous controls of sera, bile, and all antigens were included with each test. The original strains of bacteria were obtained through the courtesy of Dr. Stuart Mudd, of the Department of Bacteriology of the University of Pennsylvania.

The antigens used were *Staphylococcus aureus* (hemolytic), *B. coli*, and *B. typhosus*. These organisms were kept in stock culture on agar slants and in beef-infusion broth (pH 7.4). Stock cultures were transferred every five to six weeks. Antigens were prepared from 250 c.c. of beef infusion broth in which the organisms had been cultured for twenty-four hours at 37° C. After centrifuging, the supernatant fluid was decanted and the bacterial residue was washed twice with physiologic salt solution and was then resuspended in 25 per cent of the original volume with normal saline solution. The bacteria were killed with thymol (0.1 per cent). After twenty-four hours in the refrigerator the bacterial antigen was cultured for sterility and a smear was performed to check the bacterial content. The antigens were diluted to contain four to five billion organisms per cubic centimeter. Antigens were discarded if and when spontaneous agglutination or contamination occurred. No antigen was used for more than fifteen days. A Gram stain was performed daily on all antigens and cultures in use.

#### RESULTS

There were two main groups among the 23 patients from whom bile specimens were obtained. Sixteen patients had cholelithiasis; 7 did not. The latter group of patients were operated upon for chronic cholecystitis (3), carcinoma of the pancreas (2), heterohemolytic anemia (1), and congenital atresia of the common duct (1). Agglutinin to staphylococci, *B. coli*, and *B. typhosus* was present in the serum of all but one of the noncalculous patients, yet in no patient was the agglutinin titer greater than 1:64. Hepatic bile was obtained from 3 patients and no agglutinin was present in these specimens. Gallbladder bile was secured from 6 of these patients. Only one of these contained agglutinin and this was to the colon bacillus (1:8) (Table I).

Specimens of bile were obtained from 16 patients who had cholelithiasis. Some of these had mixed, faceted stones, while others had

TABLE I  
AGGLUTININ TITER IN PATIENTS AT OPERATION  
NO GALLSTONES PRESENT

CASE NUMBER	SERUM			GALL-BLADDER BILE			HEPATIC BILE		
	A	C	T	A	C	T	A	C	T
28729	0	0	0	0	0	0	-	-	-
31940	32	8	16	0	0	0	0	0	0
32105	12	6	6	-	-	-	0	0	0
32266	32	2	0	0	0	0	-	-	-
32637	64	0	32	0	0	0	0	0	0
32725	40	10	10	0	0	0	-	-	-
32766	64	64	16	0	8	0	-	-	-

single or multiple cholesterol stones. Agglutinin in significant titer was present in the hepatic bile of 2 of 6 patients. In each of the 12 samples of gall-bladder bile which were obtained, agglutinin to at least one bacterial antigen was present in titer of 1:16 or greater. In 11 blood specimens which were studied, the serum agglutinin was found to be of high titer (Table II).

TABLE II  
AGGLUTININ TITER IN PATIENTS AT OPERATION  
GALLSTONES PRESENT

CASE NUMBER	SERUM			GALL-BLADDER BILE			HEPATIC BILE		
	A	C	T	A	C	T	A	C	T
29135	160	80	160	128	64	128	-	-	-
31404	-	-	-	-	-	-	8	4	0
31633	320	0	20	64	0	16	-	-	-
31817	12,800	200	1,600	128	0	16	-	-	-
31848	-	-	-	-	-	-	0	0	0
31893	-	-	-	-	-	-	8	0	16
31897	-	-	-	-	-	-	0	0	0
31943	100	0	0	128	0	0	0	0	0
31950	160	20	20	12	6	0	-	-	-
32209	320	0	0	32	0	0	-	-	-
32401	1,280	40	40	32	0	0	-	-	-
32527	128	10	32	20	0	0	0	0	0
32552	1,024	64	16	64	8	0	-	-	-
32558	64	16	64	8	16	2	-	-	-
32574	64	32	32	4	16	8	-	-	-
32592	-	-	-	64	0	0	-	-	-

#### DISCUSSION

These studies are reported with the suggestion that several factors may be responsible for the formation of gallstones. They demonstrate that agglutinin is present in the bile of patients with cholelithiasis, even when almost pure cholesterol stones are found, and that agglutinin is not as a rule found in the bile of patients who do not have gallstones and who are thought to have had chronic cholecystitis.

The presence of agglutinin indicates the pre-existence of infection either in the gall bladder or elsewhere. The action of agglutinin in contact with its specific antigen may produce, as antigen-antibody

The agglutination tests were performed by serial arithmetic dilution of the serum and bile to a volume of 0.8 c.c. with isotonic buffered phosphate solution (pH 7.4) which contained 0.014 thymol. Bacterial antigen was added so that the total volume was 1 c.c. The agglutination test tubes were incubated at 37° C. for twenty-four hours and were then examined with a hand lens for evidence of agglutination. Where there was any doubt about agglutination, the test tubes were centrifuged and the sediment was resuspended in 1 c.c. of physiologic saline solution, after which they were examined again for evidence of agglutination. Simultaneous controls of sera, bile, and all antigens were included with each test. The original strains of bacterin were obtained through the courtesy of Dr. Stuart Mudd, of the Department of Bacteriology of the University of Pennsylvania.

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# NONPARASITIC SOLITARY CYST OF THE LIVER\*

## TREATMENT WITH CARNOY'S SOLUTION

BENJAMIN F. DAVIS, PH.D., M.D., DULUTH, MINN.

**N**ONPARASITIC solitary cysts of the liver are relatively rare, no more than 230 cases having been reported in the literature. It has been suggested that such cysts represent a part of the condition known as polycystic disease; however, this opinion is in the minority. The consensus is that these cysts are congenital in nature and are of biliary origin, perhaps arising from aberrant bile ducts, resulting in benign cystic adenomas.<sup>1</sup> The cysts are thin walled and contain a thin, watery liquid which, characteristically, is not bile stained. They vary greatly in size, as might be expected, the largest yet reported being the one described in this report. Microscopically, the walls consist of three layers: an outer layer of loose-meshed connective tissue, moderately vascularized; a middle layer of relatively dense fibrous tissue; and an inner layer of a single thickness of low columnar or cuboidal cells.

Clinically, the symptoms are variable, there being but one constant finding; that is, the presence of a mass. Only one case has been correctly diagnosed before operation.<sup>2</sup> The common preoperative diagnoses have been hydrops of the gall bladder, chronic cholecystitis, hydronephrosis, mesenteric cyst, ovarian cyst, and tuberculous peritonitis.<sup>1</sup>

Most of the cysts have been located on the under surface of the liver and in the neighborhood of the cleft between the lobes. There is nothing constant about the location, however. The disease may appear at any age, the most common period being between the ages of 40 and 60 years. Females are affected more often than males, in the ratio of 4 to 1.<sup>3</sup>

Treatment has been by excision, although successful results have been reported following simple drainage and marsupialization.

The chief operative complications have been hemorrhage and shock and the mortality has been rather high. Winkle and Charache,<sup>1</sup> in 1936, reported a mortality rate varying from 12 to 32.3 per cent in different series of cases and C. R. Davis,<sup>4</sup> in 1937, found reports of 50 deaths in 226 operations, a rate of 27.2 per cent.

I am reporting this case of nonparasitic solitary cyst of the liver because the condition is relatively rare, because of the unusually large size of the cyst and its unusual location, and because of the use of a sclerosing solution (Carnoy's solution<sup>5</sup>) as a means of obliterating it; this solution has been used for the obliteration of brain cysts, thyroglossal duct cysts, pilonidal cysts, and brachial cysts, but, so far as I know, it has not been used before in intraabdominal cysts.

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complex, a nidus which in itself may be a calculus or which may provide a nucleus for stone formation, particularly when the physiochemical equilibrium of the biliary constituents has been altered by disease in either the liver or gall bladder. Stone growth is more apt to occur in the presence of stasis, and such a condition more frequently occurs in the gall bladder. Although stasis is, of course, present in marked degree in carcinoma of the head of the pancreas, stone formation in this condition is rare, even though the bile salt concentration of liver from patients with this lesion may be greatly reduced. However, agglutinins were not found in the bile of the patients studied with this disease. Thus, it may well be that the coincidence of two or more factors acting in association with each other is necessary before stone formation actually takes place.

#### SUMMARY

1. Agglutinin titer for the staphylococcus, *B. coli*, and *B. typhosus* was determined in the serum, gall-bladder bile, and hepatic bile obtained at operation from a series of 23 patients.

2. In the specimens obtained from the patients who did not have gallstones, no agglutinin was present in hepatic bile; and agglutinin was present only to the colon bacillus in the gall-bladder bile of 1 of 6 patients. The serum of these patients contained bacterial agglutinin in low titer.

3. The hepatic bile in the patients with cholelithiasis contained agglutinin in 2 of 6 instances. The gall-bladder bile contained agglutinin in every one of the 12 patients with calculi. The serum agglutinin titer in these patients with gallstones was high.

4. The presence of bacterial agglutinin in patients who have cholelithiasis and the absence of bacterial agglutinin in those patients who do not have biliary calculi may be of significance in the etiology of gallstones.

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CASE REPORT.—This patient, a white female, 50 years of age, stated that, while working on a rug on June 15, 1938, she suddenly experienced a sharp, shooting pain in the region of her right clavicle. The pain radiated up the side of her neck to her head and was fairly constant but did not interfere with her sleep. She had considerable anorexia thereafter and restricted her meals to liquids on many occasions. There was no vomiting. One week later pain developed in the region of the xiphoid; this was similar to the pain in the shoulder region but more severe; it did not radiate and was not influenced by meals or by the type of food; this pain was felt more on deep inspiration. There was no coughing or spitting of blood. Some relief was obtained by strapping the chest. The diagnosis of pleurisy with gallstones was made and later another physician suggested neuritis. Three weeks after the first onset of pain, she was given x-ray treatments to the right costal margin for the neuritis, which caused considerable nausea and vomiting. About this time, she noticed a swelling in the abdomen in the region of the xiphoid.

She had never become jaundiced and her bowels had been regular up to a few days preceding the x-ray treatments. There was no fever and no chills. Past and family histories were irrelevant.

Examination at St. Luke's Hospital about four weeks after the onset of symptoms showed the following positive conditions: A mass in the right hypochondrium, with very slight tenderness. It was noted that the patient became nauseated and had severe pain in the back when lying on her back. On July 7 a gastrointestinal series and gall-bladder dye study were made. A partial quotation from the report of this examination follows: ". . . A complete examination of the gastrointestinal tract shows no evidence of pathology except a gall-bladder seat in the cap, a little four-hour retention in the stomach, and a definite appendix. The gall bladder does not fill at any time. This is undoubtedly a pathologic gall bladder with cystic duct obstruction."

Blood examination revealed nothing of significance beyond a slight anemia. The urine was normal.

The intern who made the physical examination at St. Luke's Hospital records his impressions as follows:

"(1) Pathology in the lower dorsal or upper lumbar spine?

"(2) Mass in the epigastrium?

"(3) Findings and history do not correlate very well for me. Have considered gastric carcinoma, ulcer, ventral hernia, gall-bladder disease, arthritis, mediastinal lesion (nerve injury) but I am unable to reach any conclusion."

A tentative diagnosis of gall-bladder disease was made and I was asked to see the patient. I examined her on July 11, 1938. At that time, the upper margin of liver dullness was at the third interspace anteriorly. The liver margin appeared to be one hand's breadth below the rib margin. In the area between the anterior ends of the sixth, seventh, and eighth ribs and the xiphoid was a bulging which fluctuated. I advised exploration with a probable diagnosis of subdiaphragmatic accumulation, probably secondary to gall-bladder disease.

Operation was performed July 13, 1938, under ethylene-ether anesthesia. The abdomen was opened by the Bevan S-shaped incision. Presenting in the wound was a tense fluctuating mass lying between the liver and the diaphragm, the upper surface of the liver being pushed down to about the level of the umbilicus. In addition to considerable spilling, 3,500 c.c. of watery fluid was withdrawn from the mass by suction and it was then found that we were dealing with a relatively thin-walled sac which apparently extended over the pericardium and great vessels medially, the diaphragm above and laterally, the liver inferiorly, and the abdominal wall anteriorly. That part of the sac anteriorly seemed quite fragile. Examination of the interior of the sac visually, after inserting a light, disclosed smooth, although wrinkled, walls without nodules or local thickening and no apparent source for

the liquid. A sample of the liquid sent to the laboratory was reported negative for pus and echinococcus. A portion of the sac wall was removed for microscopic study.

In view of the friability of the sac and its widespread relations, it was felt that to attempt removal was unwise; therefore, a rubber tube was inserted into the cavity and the edges of the hole in the sac were sutured to the peritoneum. The abdomen was closed in layers.

The postoperative course was relatively uneventful.

The pathologic report by Dr. Arthur Wells, on the basis of the tissue removed, stated that the sac was lined with a single layer of columnar epithelium and there were a few small glands of uniform size in the walls with cuboidal epithelium. The walls were made up of fibrous connective tissue without inflammatory reaction. The pathologic diagnosis was cyst, probably benign, probably of bile duct origin.

The drainage from the cyst, postoperatively, was quite irregular; at times there would be no drainage for twelve to twenty-four hours and then, after the patient moved around in bed, there would be an escape of a considerable quantity of watery fluid.

About four weeks after the operation, there being no apparent tendency for the cyst to close and because of the definite epithelial lining disclosed microscopically, it was felt that, unless some means of removing or destroying the lining of the sac was found, there would be a persistent sinus. A review of the literature, abstracted in the preceding pages, disclosed a disturbingly high mortality rate following attempts to enucleate such tumors. Therefore, on Aug. 9, 1938, about 80 c.c. of sclerosing fluid, known as Carnoy's solution,<sup>5</sup> was introduced into the cavity through the tube, with the patient supine, and left for four minutes; then the patient was turned on her left side for one minute, and then slowly on her right side until fluid appeared at the outer end of the drainage tube. A small catheter was then introduced through the tube and the cavity thoroughly irrigated with saline solution. This procedure was carried out with no more than a very mild psychic reaction. Carnoy's solution consists of: absolute alcohol, 60; chloroform, 30; glacial acetic acid, 10; and ferrie chloride, 10. There was moderate drainage following this treatment.

On Aug. 23, 1938, the capacity of the cavity was reduced to about 20 c.c. and at this time a second injection of sclerosing fluid was made, using the same technique as at the first injection. On Sept. 1, 1938, the drainage tube was removed. The patient was last seen on Nov. 8, 1938. The wound was healed; the patient had gained 22 pounds in weight and was apparently well.

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# THE EFFECT OF THERMAL TRAUMA ON BLOOD VOLUME, SERUM PROTEIN, AND CERTAIN BLOOD ELECTROLYTES: AN EXPERIMENTAL STUDY OF THE EFFECT OF BURNS

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THE subject of burns has been investigated extensively from many approaches. Thus, the role played by shock,<sup>1,2</sup> the bleeding volume,<sup>3</sup> adrenal disturbance,<sup>4</sup> toxins,<sup>5-8</sup> bacterial infection,<sup>9, 10</sup> fluid losses,<sup>2, 11, 12</sup> changes in blood electrolytes<sup>13</sup> and in carbohydrate and lactic acid metabolism<sup>14, 15</sup> has been studied. Investigations of the effect of severe burns on the circulating blood volume in relation to other organic changes have not been found in the literature.

The purpose of this study was to determine changes in the circulating blood volume, blood gases, hemodynamics, blood electrolytes, body fluids, and body temperature resulting from an extensive burn, and to correlate the behavior of the animal with functional changes in the renal, respiratory, and cardiac systems and with the pathologic findings at necropsy.

## MATERIAL STUDIED

Five large male and two large female normal mongrel German shepherd dogs were used. Four of these, three males and one female, were splenectomized from fourteen to thirty-three days before the experiments. The spleens were grossly normal and recovery from operation was complete prior to the experiment. Thermal trauma was applied under anesthesia to one side of the body only in Experiments 1, 2, and 5, and to both sides in Experiments 3, 6, 7, and 8, the area involving the thorax and abdomen from the level of the clavicle to the groin and laterally to the posterior axillary line.

## METHODS

Plasma and blood volumes were determined by the direct method of Gibson and Evans.<sup>16</sup> Colorimetric determination of the concentration of dye in serum samples was made with the spectrophotometer, quartz cells of 5 mm. depth being used, and 6 mg. of Evans blue were injected intravenously for each determination. With this method no correction for blood lost in sampling or from washing out of the can-

nula is necessary since the measurement obtained represents the circulating blood volume at the time of dye injection.<sup>17</sup> The hemoglobin concentration was determined by the method of Evelyn,<sup>18</sup> oxygen content and CO<sub>2</sub> content by the gasometric method of Van Slyke and Neill,<sup>19</sup> serum and urine chlorides by the method of Volhard,<sup>20</sup> serum potassium by the method of Shohl and Bennett,<sup>21</sup> serum protein by the micro Kjeldahl method,<sup>22</sup> and urine specific gravities by a gravimetric method.

#### EXPERIMENTAL PROCEDURE

Animals were fasted but given water *ad libitum* for twenty-four hours before the experiment. Anesthesia was induced by the intravenous injection of sodium pentobarbital in doses of 32.5 mg. per kilogram of body weight and maintained at adequate levels through the entire experimental period by supplementary intravenous injections of from 32.5 mg. to 97.0 mg. of pentobarbital. Animals were weighed on a lever type platform scale sensitive to 0.1 kg. prior to anesthesia and at intervals during the procedure. A continuous record of the systolic arterial pressure was obtained on the Harvard kymograph by means of a cannula inserted into the right femoral artery. Total blood lost in washing out the cannula varied from 48 to 130 c.e., averaging 80 c.e., or about 2.5 per cent of the average total blood volume. The jugular veins were exposed for ease in blood sampling. Urine samples were obtained through an indwelling catheter. After anesthesia was induced, areas of the body surface were shaved and exposed to thermal trauma by means of a Bunsen burner applied for periods of from four to twelve minutes in such a way as to produce uniform changes in the appearance of the skin throughout the area traumatized. The effectiveness of anesthesia was not altered by this procedure. Excessive heat loss by radiation from the shaved areas was prevented by covering the animal with a sheet. Rectal temperatures were taken at intervals. Arterial blood samples were taken from the left femoral artery. Tissues in the regions of the exposed vessels were kept moist with sponges wet with normal saline. Observations were made continually throughout the studies. In Experiment 1 the procedure was terminated by the intravenous injection of 170 c.e. of air and in Experiments 2, 3, and 5, of 937, 975 and 325 mg. of pentobarbital, respectively. In Experiments 6, 7, and 8 the observations were continued until the demise of the animal.

#### RESULTS

Changes in plasma, cell, and total blood volume, hematocrit, hemodynamics, blood gases, and electrolytes are shown in Table I. The relationship of these changes throughout the observation period in Experiment 7 is shown in Fig. 1.

## PLASMA VOLUME

In all cases a decrease of plasma volume occurred. A considerable decrease, amounting to 26.6, 32.1, and 36.6 per cent, in Experiments 5, 6, and 7 respectively, followed immediately after the trauma with a continued decrease at a lesser rate during the remainder of the experiment, so that the plasma volume was reduced greatly at the end of the experimental period in all cases. The degree of reduction from initial levels was somewhat greater in the splenectomized animals than in those not splenectomized. In general, the longer the experimental period, the greater was the reduction in plasma volume.

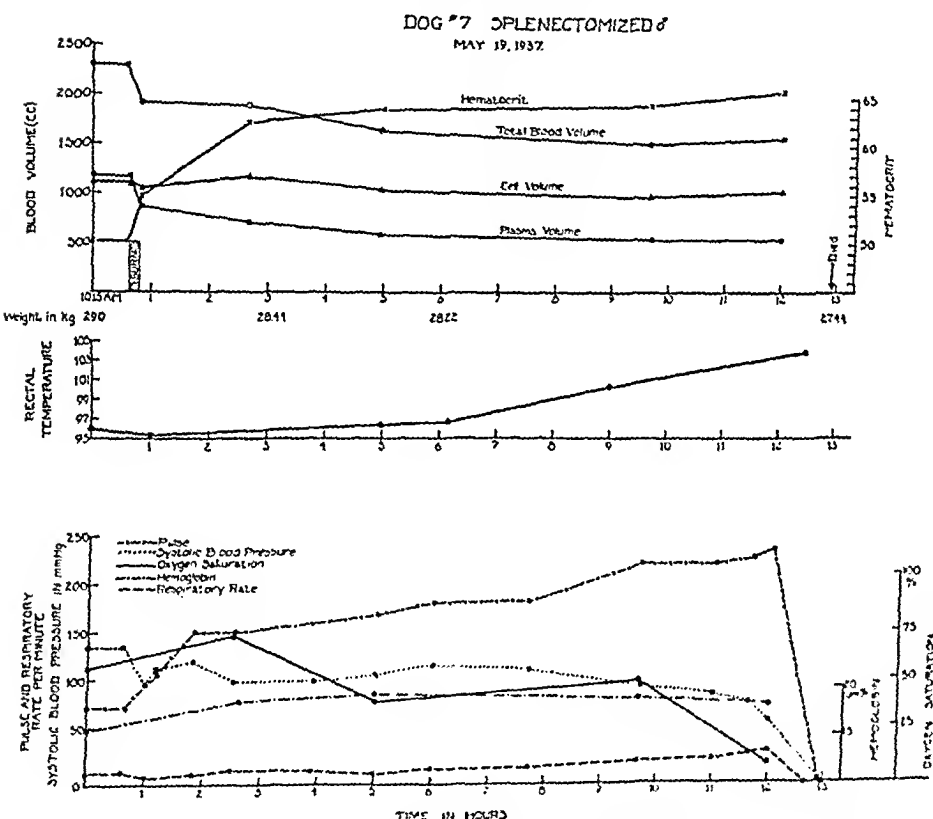


Fig. 1.—The course of changes in plasma, cell, and total blood volume, hematocrit, hemoglobin content, and oxygen saturation of venous blood; systolic blood pressure, pulse, and respiratory rates in Experiment 7.

## RED CELL VOLUME

A marked contrast in the course of the circulating red cell volume was observed between the nonsplenectomized and splenectomized animals. Thus, in Experiments 1, 2, and 3 there was a marked increase in the total volume of the circulating red cells. This increase occurred

shortly following thermal trauma, and there was a general tendency for this increase to be sustained throughout the course of the experimental period. The circulating red cell volume was increased 59.5, 24.6, and 22.3 per cent above initial levels in Experiments 1, 2, and 3 respectively.

In the four splenectomized animals the circulating red cell volume decreased, there having been a reduction of 27.8, 7.8, and 13.1 per cent in Experiments 6, 7, and 8 respectively and little change in Experiment 5.

#### TOTAL BLOOD VOLUME

A marked difference in the course of total blood volume was observed in the nonsplenectomized and splenectomized animals due to the different response of the red cell volume, there being slight increases and only moderate decreases in the nonsplenectomized animals but considerable reductions in the splenectomized animals. The greatest reduction in total blood volume in nonsplenectomized animals occurred in Experiment 2, amounting to 20.6 per cent. The characteristic course of total blood volume in the splenectomized animals was a progressive reduction, amounting to 33.6, 41.6, and 30.8 per cent in Experiments 5, 6, and 7 respectively at the end of the experimental period.

#### HEMODYNAMICS

The initial pulse rate varied considerably in the different animals, but in general there was a tendency for the pulse rate to rise gradually as the experiment progressed, with a sharp rise to very high levels terminally. Initial blood pressures also varied considerably. During the course of the thermal trauma arterial pressure dropped sharply, as much as 70 mm. of mercury in Experiments 3 and 8. This fall in pressure was accompanied by a rise in pulse rate and little change in respiratory rate. Following trauma, the arterial pressure tended to return to the initial level. In the three nonsplenectomized animals the initial level was maintained throughout the experimental period. In the four splenectomized animals, following the recovery from the reduction accompanying the thermal trauma, there was a gradual and steady fall. In Experiment 5 systolic pressure was 40 mm. of mercury at the time the experiment was terminated by the intravenous injection of pentobarbital. In Experiments 6, 7, and 8 death occurred at nine, thirteen, and nine hours after thermal trauma and shortly before demise the systolic pressure fell sharply. In these three animals the terminal fall in pressure was preceded by a marked increase in the respiratory rate which was 120 per minute in Experiment 8 shortly before death.





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## BLOOD GASES, SODIUM CHLORIDE, AND SERUM PROTEIN

OXYGEN (VOL. %)	HEMOGLOBIN (GM. %)	OXYGEN CAPACITY (VOL. %)	OXYGEN SATURATION (%)	CARBON DIOXIDE (VOL. %)	SERUM NaCl (MG. %)	SERUM K <sup>+</sup> (MG. %)	SERUM PROTEIN (GM. %)	REMARKS
<i>March 7, 1937</i>								
13.8	16.05	21.52	64.2	-	-	18.65	-	Burned, left side only, 6:24-6:37 P.M.
15.1	17.95	24.03	63.0	-	734	18.65	7.96	
13.7	19.1	25.60	53.5	-	783	18.65	7.88	Burned, left side only, 9:18-9:22 P.M.
7.0	19.81	26.55	26.9	-	763	22.95	7.55	170 e.e. air intravenously at 3:00 A.M.
12.5	21.65	29.05	43.0	-	724	17.02	7.36	Dead at 3:32 A.M.
<i>March 22, 1937</i>								
13.94	14.68	19.65	70.9	45.9	734	14.05	6.32	Burned, left side only, 11:09-11:17 A.M.
16.12	17.00	22.08	70.7	48.1	734	14.05	6.42	Harsh systolic murmur developed over
16.56	18.35	25.91	63.9	45.9	743	14.05	6.40	apex at 12:10 P.M.
13.76	20.40	27.40	50.2	45.8	734	11.24	6.35	
13.65	22.3	29.90	45.7	45.3	754	16.85	6.17	910 mg. pentobarbital at 9:41 P.M.
<i>April 5, 1937</i>								
16.3	18.62	24.98	65.2	-	694	15.2	7.22	Dead at 9:50 P.M.
11.44	18.4	24.65	46.4	-	724	-	7.85	Burned, left side, 11:46-11:50 A.M.
8.82	21.15	28.2	31.27	-	714	16.1	7.66	Burned, right side, 11:56-12:05 P.M.
16.34	23.6	31.68	51.5	-	754	15.8	7.04	650 mg. pentobarbital intravenously at
<i>Splenectomized April 2, 1937</i>								
-	-	-	-	-	-	-	-	8:55 P.M.
8.71	17.45	23.4	37.2	641	-	6.31	-	Dead at 9:40 P.M.
6.24	19.35	24.1	24.1	-	-	-	-	Burned, left side only, 10:31-10:41
1.53	19.85	26.55	5.76	623	-	7.00	-	A.M.
<i>Splenectomized April 2, 1937</i>								
-	-	-	-	473	-	7.02	-	325 mg. pentobarbital 11:07 P.M.
7.48	16.20	21.75	34.4	-	-	-	-	Dead at 11:12 P.M.
3.30	17.70	23.65	13.95	-	-	-	-	Burned, left side, 11:45-11:51 A.M.
1.65	23.15	31.05	5.32	-	-	-	-	Burned, right side, 11:51-11:56 A.M.
0.26	24.13	32.35	0.81	-	-	-	-	
-	23.70	31.80	-	-	-	-	-	Dead at 6:57 P.M.

TABLE I—

TIME (HR., MIN.)	WEIGHT (KG.)	RECTAL TEM- PERATURE (° F.)	BLOOD VOLUME						HEMATOCRIT (VOL. %)	PULSE (PER MIN.)	SYSTOLIC BLOOD PRESSURE (MM. Hg)	RESPIRATIONS (PER MIN.)
			PLASMA (C.C.)	% CHANGE	CELL (C.C.)	% CHANGE	TOTAL BLOOD (C.C.)	% CHANGE				

*Dog 7.—May 19, 1937.*

Initial												
10:15 A.M.	28.94	96.0	1170		1125		2295		50.5	72	132	13
1 00	-	95.2	748	-36.6	962	23.4	1770	-22.9	57.7	150	96	16
2 40	28.44	95.4	715	-38.9	1180	+ 4.9	1895	-17.3	62.3	158	98	14
4 57	28.22	96.3	598	-48.8	1047	- 6.9	1645	-28.3	63.7	168	110	12
9 42	-	101.0	543	-53.5	977	-12.8	1520	-33.7	64.2	222	96	24
12 01	27.44	103.4	543	-53.5	1037	- 7.8	1580	-30.8	65.7	234	54	32

*Dog 8.—July 9, 1938.*

Initial										120	140	17
10:05 A.M.	24.18	101.4	1050		1220		2270		55.0			
0 50	-	102.7	-		-		-			142	120	100
2 28	23.40	104.2	875	-16.65	1130	- 7.37	2005	- 11.65	56.5			
6 46	23.20	106.2	770	-26.7	1060	-13.1	1935	- 1.46	60.3	194	140	70
7 25	-	106.6	-	-	-	-	-	-	-			
8 41	23.20	106.6	-	-	-	-	-	-	-	214	120	120
										244	98	90
										254	70	76

## BLOOD GASES

Accompanying the increasing hematocrit values there was a consistent increase in the hemoglobin concentration of the blood in all cases, greater in the nonsplenectomized than in the splenectomized animals. The oxygen content of venous blood fluctuated somewhat in a manner parallel to the changes in the circulating red cell volume. In only two nonsplenectomized animals, 1 and 3, were low values observed. In all of the splenectomized animals there was a marked and progressive decrease in the oxygen content of the venous blood, terminal values of less than three volumes per cent being observed in Experiments 6, 7, and 8.

Due to the increase in oxygen capacity resulting from the rise in hemoglobin concentration and to the decrease in oxygen content, the oxygen saturation fell, terminal values of 43, 45.7, and 51.5 per cent having been observed in nonsplenectomized Animals 1, 2, and 3, in all of which the experiment purposely was terminated. The decrease in oxygen saturation was much more pronounced in the splenectomized than in the nonsplenectomized animals, in that initial levels were lower and the oxygen saturation fell more rapidly and to lower levels. In

CONT'D

OXYGEN (VOL. %)	HEMOGLOBIN (GM. %)	OXYGEN CAPACITY (VOL. %)	OXYGEN SATURA- TION (%)	CARBON DIOXIDE (VOL. %)	SERUM NaCl (MG. %)	SERUM K+ (MG. %)	SERUM PROTEIN (GM. %)	REMARKS
<i>Splenectomized March 24, 1937</i>								
11.16	14.78	19.8	56.6	54.0	692	15.0	7.40	Left side burned 10:48-10:53 A.M.
-	-	-	-	-	-	-	-	Right side burned 10:53-10:57 A.M.
16.77	17.70	23.70	70.7	45.7	-	-	-	
9.82	18.40	24.65	39.8	38.5	698	15.0	7.21	
11.67	17.85	23.95	48.8	38.0	706	14.8	6.80	
2.30	17.15	23.0	10.0	52.0	-	-	6.80	Died at 11:04 P.M.
<i>Splenectomized June 21, 1938</i>								
A 13.0	17.48	23.4	55.5	44.5	609	-	6.49	Burned, left side, 10:38-10:44 A.M.
V 11.0	17.48	23.4	48.0	45.5				Burned, right side, 10:44-10:49 A.M.
A 16.2	19.8	26.6	62.3	43.0				
V 15.4	20.4	24.35	56.3	44.5				
A 11.5	18.4	24.65	47.9	46.0	659		6.77	
V 10.9	18.4	24.65	44.2	48.0				
A 8.4	19.35	26.0	32.3	39.0	659		5.88	
V 7.8	19.61	26.3	29.6	40.0				
A 6.4	20.6	27.6	23.1	24.0				
V 5.2	20.4	27.35	19.0	27.4				
A 3.7	21.8	29.2	12.75	50.0				Died at 6:52 P.M.
V 2.9	22.0	29.5	9.83	51.0				

Experiments 6, 7, and 8, which succumbed to the experimental procedure, oxygen saturation was less than 10 per cent just prior to demise. The carbon dioxide content of venous blood changed but little in non-splenectomized animals, the value in the terminal blood sample being about the same as the initial level. In the splenectomized animals there was some lowering of the carbon dioxide content as the experiment progressed, with a terminal rise as respiration failed. A parallel between the lowering of the carbon dioxide content of venous blood and the terminal rise in the respiratory rate was observed.

#### BLOOD ELECTROLYTES

The concentration of sodium chloride in the blood serum varied little, but, due to the decrease in plasma volume occurring during the experiment, the total amount of this salt present in the circulating blood stream was reduced greatly at the end of the experiment, even in those cases in which the total blood volume was little changed (Experiments 1, 2, and 3). The concentration of serum protein was within normal limits in all experiments, but there was a tendency for the concentration to fall as the experiment progressed, which, when considered in the light of the reduction in plasma volume, indi-

cates a considerable loss of protein from the blood stream. In the experiments in which blood potassium was determined, the concentrations were within normal limits and the variations observed bore no relationship to the duration of the experiment, changes in blood volume, or eventual collapse of the circulation.

#### PATHOLOGIC FINDINGS

Neeropsies were completed within two hours of death. At post mortem in the animals traumatized on one side only paper patterns of the burned areas were obtained for comparison of the amount of surface area involved on the normal and affected sides. In these animals the skin and subcutaneous tissues over the burned area were excised and the weight of this tissue mass compared with the weight of a corresponding area of skin and subcutaneous tissue excised from the normal side as a basis for the estimation of the amount of fluid extravasated into the burned area.

The post-mortem findings in all animals were essentially similar. There was severe dehydration, the tissues, muscles, and serous surfaces all being exceedingly dry. There was practically no fluid in any of the serous cavities, nor was there any "pooling" of blood in vessels or organs in the abdominal area.

On opening the body, the cut surfaces of the traumatized area bulged, revealing a gelatinous, edematous mass beneath the skin, somewhat hemorrhagic and of a greenish tinge, undoubtedly due to staining with the Evans blue. Microscopically there was coagulation necrosis of the skin surface and marked edema and occasional areas of necrosis in the subcutaneous tissues, as evidenced by infiltration by polymorphonuclear leucocytes. The chest was contracted and narrowed, and the diaphragms were high. The lungs were collapsed, lying against the posterior thoracic wall, a light pink in color, very dry and containing little air, microscopically showing only slight engorgement of the capillaries in the alveolar walls. The bronchi contained no mucus. In the lower portions of the lungs posteriorly there were frequent areas of purple color, firm and noncrepitant, from the cut surfaces of which air could be expressed. These sections showed, in addition to engorgement of the alveolar wall, infiltration with polymorphonuclear leucocytes and a marked decrease in the size of the alveolar spaces, the picture being similar to an early bronchial pneumonia of the type seen in childhood. The peribronchial lymph glands were greenish in color, due to staining with the dye.

The pericardium and epicardium were glistening and dry, and a few cubic centimeters of thin yellow serous fluid were found in the pericardial cavity. The heart muscle was firm in some instances and slightly flabby in others, but no involvement of the coronary arteries

was found, and, on section, the cut surface of the ventricle was dry and somewhat granular. Microscopically there were no significant morphologic changes in the heart muscle. The valves were normal in all animals except Experiment 3 in which there was an ulcerated lesion on the posterior cusp of the mitral valve about 9 mm. in diameter with sharply demarcated margins and great thinning of the cusp centrally. This dog developed a loud harsh systolic murmur during the course of the experiment. The aorta appeared normal, as did the esophagus and vena cava, which contained very dark, nonclotted blood.

The abdomen was seaphoid. There was no gross evidence of infection at the site of the insertion of the cannula into the femoral artery. The peritoneal surfaces everywhere were dry and glazed looking, and there was no free fluid in the peritoneal cavity. The omentum was in normal position, waxy in appearance, and the mesenteric vessels were narrowed and poorly filled. In general, there was marked ischemia of the entire gastrointestinal tract, the stomach and bowel being pale and practically empty and contracted, except for the rectal ampulla. The rugae of the stomach were elevated with hyperemic summits. There were no frank ulcers in the stomach. The mucosa of the entire small bowel showed varying degrees of hyperemia, with definite ulcerations in the duodenum and jejunum of two animals. Microscopically the pink ulceration was superficial, but there was an area of necrosis as evidenced by a change in the staining property that extended to the submucosa. The linear folds of the colon were reddened, especially in the lower portions. In some animals the fecal contents of the rectal ampulla were grossly blood stained.

The liver surface was smooth, brown in color, and dry. On section little blood could be expressed from the cut surface, which had a somewhat nutmeg appearance. There was no gross necrosis. Microscopically there were scattered areas of engorgement of the sinusoids around the central vein, with some central necrosis as evidenced by polymorphonuclear leucocytic infiltration. The gall bladder was normal in size, and the bile was a greenish brown in color and seemed normal in amount.

The pancreas was dry, pale, and on section the surface was pale and waxy with scattered red punctate areas. There were no abnormalities microscopically.

In the three animals which were not splenectomized, the spleen was contracted, firm, blue in color with scattered raised purple areas on the surface. On section the pulp seemed very friable, and but little blood could be expressed from the cut surface.

The kidneys were firm, normal in size, blue-green in color. The capsule stripped easily and, on section, the cortex was a deep purple with prominent markings. The pyramids were a pink-purple color,

the pelves normal. Microscopically there was albuminous material within the capsular spaces of the glomeruli, and occasional hyaline and granular casts were seen in the convoluted tubules. Colloid degeneration of the convoluted tubules, the cells of which also contained some hemosiderin, was seen. Ureters were normal. The bladder was empty, contracted, very firm, and there was slight hyperemia of the mucosa but no ulceration, hemorrhages, or calculi.

The adrenals were ivory white, very dry and firm. On section no gross abnormalities of either cortical or medullary portions were evident. In all instances, however, microscopic examination revealed invasion of the cortex by polymorphonuclear leucocytes, involving the zona fasciculata principally and to a lesser extent the zona reticularis. These lesions are illustrated in Fig. 2. In only one adrenal was there even slight polymorphonuclear invasion of the zona glomerulosa, and this was limited to one small area immediately adjacent to the damaged area in the cortex.

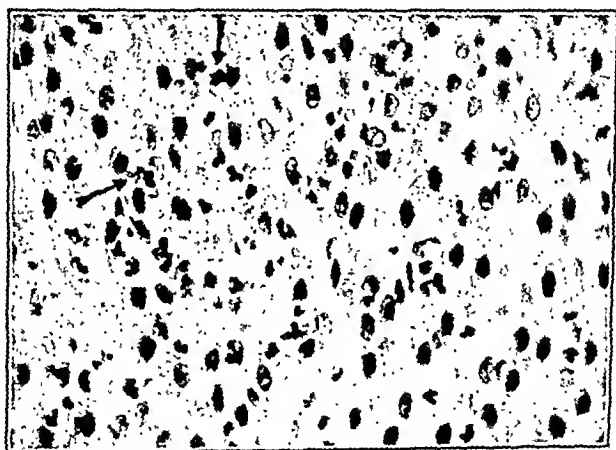


Fig. 2.—Lesions in the adrenal cortex. Section of adrenal from Experiment 7 ( $\times 70$ ), hematoxylin and eosin stain, shows the region of the zona fasciculata in which the infiltration with polymorphonuclear cells is most intense. The leucocytes are seen lying between the cortical cells and, in the areas indicated by the arrows, within the cortical cells.

Grossly the membranes of the brain were smooth and glistening, the dura was intact, and there was no evidence externally of any gross hemorrhage. There was little fluid in the subarachnoid spaces. The hypophysis appeared normal and was not stained by the dye.

Histologic studies of the brain of Experiment 8 showed evidence of a diffuse circulatory disturbance. Sections stained by the benzidine technique of Lepehne and Pickworth prepared according to Method 2 in the modification employed by Doherty, Suh, and Alexander<sup>21</sup> showed the entire vascular bed to be congested, the vessels being densely packed with red blood corpuscles, without, however, any marked

dilation. There was some "bead" deformity of the vessels, especially those near hemorrhagic areas. Scattered throughout the brain were small hemorrhages, ranging in severity from perivascular sheath hemorrhages to small perivascular and parenchymatous hemorrhages with extravasation of red cells into the adjacent brain tissue, being most frequently found in the bases of the hemispheres, notably in the prepyriform and entorhinal areas, in the medial and dorsal portion of the thalamus, around the aqueduct of Sylvius, in the corpus callosum, and in the white matter of the cerebellum. These changes are shown in Fig. 3.

In Experiment 2 sections stained by the technique of Masson and Mallory confirmed the findings in Experiment 8, there being dense packing of the vessels with small perivascular and parenchymatous hemorrhages in similar regions with "bead" deformity of some of the vessels.

No cellular damage was seen in any of the brains examined, the cell nuclei everywhere being pale and clear and the cell margins and dendritic processes being sharply defined, nor was there any evidence of glial damage or proliferation.

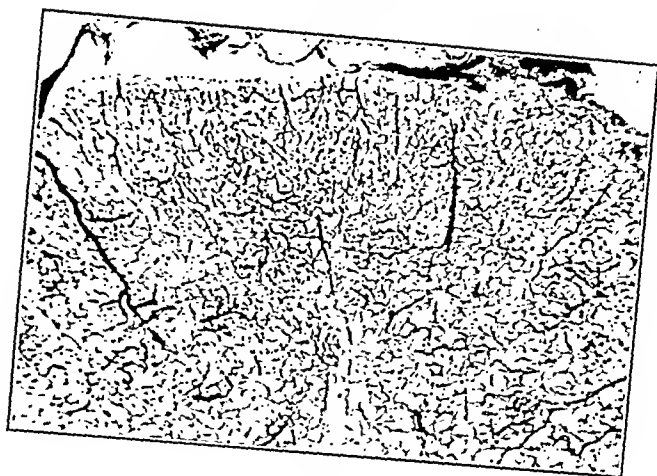
In Experiment 6 evidence of healed previous brain damage, characterized by organization of previous perivascular hemorrhages with thickening of the adventitia and perivascular lymphocytic infiltration, was found. These lesions were obviously old and could have had no relation to the trauma under investigation. In this animal, however, fresh hemorrhages of the type described above were found in the region of the aqueduct of Sylvius.

#### DISCUSSION

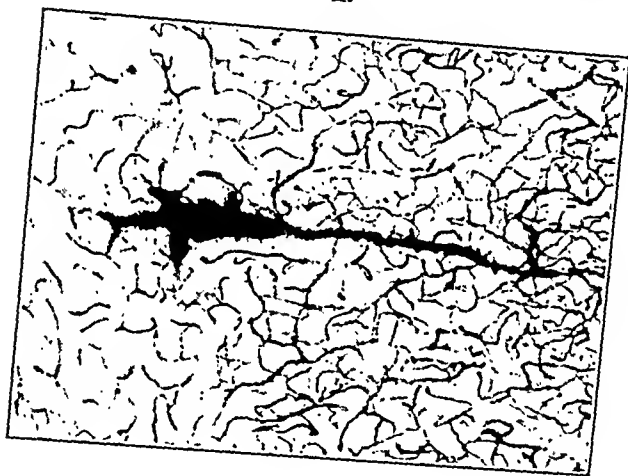
The striking characteristic of the behavior of the circulation in these animals was the maintenance for long periods of arterial blood pressure well above shock levels, even though the animals were severely traumatized. However, demise was due to a complete breakdown of the respiratory and vascular mechanisms, and the extent to which the observed changes contributed to this collapse may be of significance in the consideration of the causes of death in burns.

All of these animals experienced drastic reductions in circulating plasma volume. It may be argued that the presence of a large area with extensive capillary damage might influence the disappearance of the dye from the blood stream and hence the accuracy of the plasma volume determinations. With the exception of values obtained in Experiments 5, 6, and 7 by the short indirect method<sup>16</sup> immediately following the thermal trauma, all of the plasma volume determinations were made with individual dye injections. In a previous communication<sup>17</sup> it was pointed out that the plasma volume, since it is based upon the dye dilution value obtained by the extrapolation of the slope of





A.



B.



C.

Fig. 3.—Lesions in the brain. Sections are of fresh material from Experiment 8, stained by the benzidine technique of Lepehne and Piekworth to show the vascular bed. A, Occipital cortex ( $\times 24$ ). There is marked congestion. The capillary bed is composed largely of loops rather than straight branching vessels. The vessels are densely packed with red cells but not dilated, averaging  $6\ \mu$  in diameter. B, Area entorhinalis ( $\times 70$ ). A perivascular sheath hemorrhage in a severely congested cerebral vascular bed is shown. C, Corpus callosum ( $\times 60$ ). A small perivascular hemorrhage with extravasation of red cells into the parenchyma of the brain is shown. These lesions are evidence of congestion and stasis in the cerebral vascular bed and hence of some degree of anoxia of brain tissue.

disappearance of the dye from the blood stream to the time of injection, represents the plasma volume existing at the time of injection, and the accuracy of the result is but little influenced by variations in the rate of dye disappearance. Hence the recorded values are reliable.

These reductions in plasma volume resulted from large uncompensated losses of body fluids. In Table II are shown the losses in plasma volume and of tissue fluid into the damaged areas. In this analysis it is assumed that all weight lost may be regarded in terms of body fluid and that all body fluid lost either from the lungs and kidneys or as edema must have passed through the circulating blood stream. Total fluid loss is, therefore, equal to the weight loss plus the weight of the edema fluid, and tissue fluid loss is equal to total fluid loss minus the reduction in plasma volume. Total fluid loss, of which the greater portion was tissue fluid, was 7.24, 7.29, and 6.08 c.c. per hour per kilogram of body weight in Experiments 1, 2, and 5 respectively.

TABLE II  
TOTAL FLUID AND TISSUE FLUID LOSSES

EXPERIMENT NO.	WEIGHT (KG.)	WEIGHT LOSS (GM.)	URINE OUTPUT (C.C.)	FLUID LOSS FROM LUNGS (C.C.)	FLUID LOSS INTO DAMAGED AREA (C.C.)	TOTAL FLUID LOSS		REDUCTION IN PLASMA VOLUME (C.C.)	TISSUE FLUID LOSS (C.C.)
						(C.C.)	(C.C.) PER HR. PER KG.		
1	19.65	450	75	375	960	1,410	7.24	284	1,126
2	32.3	1,210	67	1,143	1,160	2,370	7.29	645	1,725
5	22.44	580	63	517	900	1,480	6.08	608	872

It was observed that the rate of disappearance of the dye was more rapid in the early determinations than in those carried out near the end of the experiments, and we regard this as evidence that in the latter part of the experimental period less and less fluid was passing from the blood stream into the traumatized area. This is in keeping with the observation that the greater part of the swelling in the traumatized areas occurred very shortly after thermal trauma. That the plasma volume remained reduced during the latter portion of the experiments, even though the rate of extravasation of fluid into the damaged area was diminished, is evidence of exhaustion of the body fluid reserve. Further evidence of the severity of the dehydration is the almost complete anuria which developed in all these animals, together with the rise in the specific gravity of the urine, even during periods when the systolic blood pressure was well sustained (Table III).

Total blood volume was sustained at very nearly initial levels in the three nonsplenectomized animals, 1, 2, and 3, in spite of the reduction in plasma volume, by a large increase in the volume of circulating red cells. No marked fall in the systolic blood pressure was observed, and it seemed evident that these animals could have survived beyond

TABLE III

SPECIFIC GRAVITY AND CHLORIDE CONTENT OF URINE  
EXPERIMENT 8

TIME (HR., MIN.)	AMOUNT (C.C.)	SPECIFIC GRAVITY	CHLORIDE CONTENT (GM. VOL.)
9:30 A.M. July 9, 1938	13	1.045	.0416
20	12	1.047	.0408
45	22	1.050	.0380
1 31	12	1.050	.0024
2 22	13	1.043	.0013
2 50	5	1.066	.0
5 24	4	1.090	.0
8 31	12	1.075	.0

the induced end of the experiment. In these animals the oxygen content of venous blood was well sustained and, while there was a fall in oxygen saturation, it seems evident that the oxygen-carrying mechanism was functioning fairly adequately since respiratory rates did not rise markedly nor did venous carbon dioxide content fall appreciably. In marked contrast to this situation the total blood volume of the splenectomized animals progressively decreased throughout the experiment, having been reduced 33.6, 41.6, and 30.8 per cent from initial levels at the time of death in Experiments 5, 6, and 7 respectively. In the splenectomized animals the percentage reduction in plasma volume was somewhat greater than in the nonsplenectomized animals, but the reduction in red cell volume was chiefly responsible for the marked reduction in total blood volume. In these animals systolic blood pressure, in general, paralleled the course of total blood volume, gradually falling as the experiment was continued until, in Animals 6, 7 and 8, when levels of from 50 to 70 mm. of mercury were reached, there was a rapid and fatal circulatory collapse preceded by a sharp rise in respiratory rate. Just prior to collapse, the total blood volume was reduced 41.6 and 30.8 per cent in Experiments 6 and 7 respectively.

With the increase in hematocrit, there was an increase in the hemoglobin concentration and, therefore, in the oxygen capacity, less marked in the splenectomized than in the nonsplenectomized animals. Venous oxygen content, however, fell progressively to extremely low levels, the oxygen saturation being less than 10 per cent at the time fatal collapse occurred in Experiments 6, 7, and 8. It is evident that the efficiency of the oxygen-carrying mechanism in these animals was seriously impaired. Respiratory rates rose rapidly prior to collapse and venous  $\text{CO}_2$  values fell in relation to the increase in respiratory rate.

No marked change in concentration of serum chlorides occurred, but due to large reductions in plasma volume the total amount present in the circulation was greatly lowered. This indicated a large loss of

sodium chloride into the burned area. The concentration of serum protein was diminished terminally in five of the six experiments in which serum protein determinations were done. Here again, due to decrease in plasma volume, the total amount of serum protein was greatly reduced. On the basis of estimation of the amount of fluid (Table II) extravasating into the traumatized area, assuming the protein content of the edema fluid to be approximately equal to that of the blood serum at the time of injury,<sup>24</sup> we compute that the loss of protein into the damaged area was far greater than the reduction in the amount of serum protein in the circulating blood volume. This fact strongly suggests that, in these animals, there existed a source of proteins available for rapid mobilization.

No significant change in concentration of blood potassium occurred, although considerable amounts may have been lost into the damaged areas.

While no determinations of the pH of the blood were made, it is probable that no severe degree of acidosis developed in the non-spleneetomized animals in which respiratory rates were not markedly accelerated, and in which venous CO<sub>2</sub> values and chloride concentrations were normal, but there may have been moderate acidosis terminally in the spleneetomized animals.

Several factors must be considered as bringing about the peripheral vascular collapse seen in these animals. Reduction in blood volume with the disparity between volume capacity and circulating blood volume described by Moon<sup>25</sup> is known to produce peripheral collapse. Exactly this picture was described by Gibson and Kopp<sup>26</sup> in patients undergoing artificial fever treatments in whom severe reductions in blood volume preceded profound vascular collapse. It was observed that, as the experiments progressed, there was very little blood in the large peripheral veins, the jugular vein exposed for sampling being partially collapsed. The poor venous return manifested by this lowering of venous pressure could not but aid in the development of cardiovascular failure. It should be said, however, that in all animals in which death occurred respiration was the first to fail, the heart continuing to beat for several minutes after the complete cessation of respiration.

In all the animals which succumbed, a profound anoxia, as evidenced by extraordinarily low oxygen saturations of venous blood, was observed prior to collapse, even though the respiratory rate was markedly elevated at this time. It is hardly possible that the oxygen tension in the tissues, and particularly in the brains, of these animals could have been adequate for proper oxygenation of cells.

In the opinion of Dr. Leo Alexander the perivascular and parenchymatous hemorrhages seen in Experiments 2, 6, and 8 are fresh, and it is reasonable to assume that in point of time they are related

to the duration of the experiment and that they may be considered as evidence of the existence of areas of stasis in a severely congested cerebral vascular bed.

In an effort to evaluate the influence of anesthesia on brain tissue, a control experiment was done using a normal, healthy male shepherd dog weighing 19.1 kg. Anesthesia was induced by the intravenous administration of 32.5 mg. of pentobarbital (nembutal) per kilogram of body weight and was maintained by supplementary doses for a period of ten hours. The animal was then sacrificed by an additional intravenous injection of 975 mg. of pentobarbital, and the brain was removed immediately for study. The sections of the brain of the control animals showed hemorrhages similar to those seen in the brains of the animals subjected to thermal trauma. One significant difference existed. The sections from the control animal showed capillary dilatation in addition to the hemorrhages; whereas, the sections from the traumatized animals demonstrated capillaries of normal size. It is suggested that the degree of dehydration present in the thermally traumatized animals counteracted the vasodilatory effect of pentobarbital. No areas of injury to motor or ganglion cells of the kind described by Gildea and Cobb<sup>27</sup> were observed. It is possible, however, that there may have been some functional damage to nerve cells, since death occurred suddenly, and there may have been insufficient time for the development of morphologic changes.

Although the vascular lesions in the brains of the experimental animals cannot be attributed entirely to the effects of thermal trauma, it is probable that the degree of anoxia, as evidenced by the amount of congestion and the frequency of the lesions, was more severe, and the functional damage to nerve cells was greater in the experimental than in the control animal.

Microscopically the adrenals showed damage to the cortical areas characterized by infiltration with polymorphonuclear leucocytes, to a marked extent in the zona fascicularis and to a less extent in the zona reticularis. The adrenals of a control animal, subjected to nine hours of anesthesia with pentobarbital, showed no abnormalities microscopically. Lesions similar to those seen in the adrenal cortex of these animals have been described by Hartman<sup>28</sup> in animals which died following artificial hyperpyrexia. However, our experiments were acute and sufficient time may not have elapsed for the development of morphologic changes in the adrenal medulla. Blood potassium levels were not particularly elevated beyond levels that might result from hemoconcentration and, what changes did occur, probably were of no significance in the production of vascular collapse. Adrenal damage was very probably not of primary importance but cannot be excluded as playing some role in the development of shock in these animals.

The continuous anesthesia maintained throughout these experiments had the effect of minimizing the part played in burns by reactions to painful stimuli and in our opinion afforded an opportunity to study the changes in the vascular and respiratory systems in the absence of a primary neurogenic factor.

No evidences of infection in the traumatized areas or elsewhere were found at post mortem, and it is, therefore, highly improbable that toxins of bacterial origin played any part in the reaction of the animals.<sup>9</sup> The effect of toxins possibly released from damaged tissue, however, cannot be excluded.<sup>8</sup>

All of the animals had some degree of elevation of body temperature, but in no case was there a rise to fatal levels. The significant effect of the fever probably was an increase in metabolism, as has been shown to occur in typhoid fever by Dubois<sup>29</sup> and in artificially induced fever by Bazett.<sup>30</sup> As a result, the oxygen requirement of these animals must have been increased. With increase in body temperature and oxygen consumption, heat production increases and, since these animals lost heat principally by evaporation of the water content of alveolar air, an increase in the loss of body fluid resulted.

It is evident that no single one of the above factors was solely responsible for the shock which terminated the existence of these animals, but that shock occurred as the result of the final failure of the organism to contend with certain primary reactions to the trauma sustained and secondary disturbances following inevitably in the train thereof. The train of events leading to the establishment of a vicious cycle may be described as follows:

#### *Primary Reactions.—*

1. As a result of alterations of the permeability of the capillaries in the traumatized tissues there is an immediate and considerable extravasation of fluid, which may be considered as slightly diluted blood serum containing many red cells, into the damaged area.

2. Since this fluid is withdrawn directly from the blood stream, an immediate and considerable reduction in the circulating plasma volume results, bringing about, in addition to a lowering of the total blood volume, a marked hemoconcentration.

3. A rise in body temperature occurs, due primarily to the thermal input accompanying the application of heat and secondarily to an increase in body heat production, and with this an increase in the oxygen consumption.

#### *Compensatory Reactions.—*

4. Extracellular fluid moves into the circulating blood stream in obedience to the laws of electrolytic equilibrium and partially replaces fluid losses from the plasma.

5. As the oxygen requirement increases and the oxygen saturation falls (see No. 7 below), respiratory activity becomes increased, so that the rate of fluid loss from the lungs increases, imposes an additional drain upon the fluid reserve, and brings about further decreases in plasma volume, further hemoconcentration, and a tendency toward an acidosis.

6. The hemoconcentration brought about by reduction in the plasma volume is augmented by a considerable increase in the total volume of the circulating red cells. The increased viscosity of the blood resulting therefrom acts as an impedanee to blood movement and impairs gas exchange between tissues and blood. When the available reserve of red cells is exhausted, continued fluid loss brings about a further reduction in total volume.

7. As a result of hemoconcentration, acidosis, and slowed blood flow through the lungs, oxygenation of arterial blood becomes increasingly inefficient, tissue anoxia with a compensatory hyperventilation occurs, and the rate of fluid loss, consequent reduction in plasma volume, and hemoconcentration increase.

In the vicious cycle thus established a point is reached eventually at which the circulating volume is no longer adequate for maintenance of venous return to the right heart, and cardiac function suffers. At the same time tissue anoxia in the brain produces paralysis of respiratory and vasomotor centers with, finally, sudden fatal collapse.

Several conclusions of clinical interest as regards the treatment of severe burns in human beings may be drawn from the above discussion. It is clear that the chief factor in initiating the train of events leading to collapse was the severe and progressive dehydration suffered by these animals. The amount of fluid that can be lost into a severely burned area and the speed with which this loss can take place are striking and emphasize the urgent need for prompt and adequate fluid replacement. The chief effect of an uncompensated loss of fluid into the affected area is a reduction in the plasma volume. It is the consequent hemoconcentration which interferes with the speed of blood flow and with oxygenation that leads inevitably to the vicious cycle of continued fluid loss, hyperventilation, anoxia, acidosis, and eventual respiratory and circulatory failure. Some idea of the amount of fluid required by a severely burned patient can be obtained from a consideration of the total tissue fluid losses of these animals. The loss of tissue fluid was 7.2, 6.56, and 4.57 c.e. per hour per kilogram of body weight in Experiments 1, 2, and 5 respectively, or amounts equal to about one and one-half times the normal plasma volume. Thus, in the case of a man weighing 70 kg. with a severe burn involving about a third of the body surface, based on a tissue fluid loss at the rate of only 5 c.e. per hour per kilogram, the twenty-four-hour fluid requirement would be 8,400 c.e. This conjecture is in keeping with the re-

peated clinical observation that severely burned patients can be given large amounts of fluid parenterally without producing much improvement in blood pressure or clinical state. In addition, it should be remembered that, since the human mechanism for heat dissipation is, to a great extent, dependent upon evaporation of water from the skin, fluid losses in patients with even slight fever may well be in excess of those experienced by these animals. The relatively bloodless and contracted state of the entire intestinal tract seen in these animals would suggest also that water absorption from the stomach and bowel might be impaired in severely burned patients and serve as a good basis for the parenteral administration of fluids, even in large amounts.

The beneficial effect of transfusions in burned patients in all probability is due as much to the additional oxygen carrying material thus supplied as to the replacement of lost serum protein and blood electrolytes. Thus, the animals that could transfuse themselves from their own spleens tolerated the trauma and reactions thereto far better than did the splenectomized animals in which the reserve of available red cells was limited.

A sharp and sudden rise in hemoglobin or red cell count in burned patients should be regarded as an indication for further administration of fluids or for transfusion.

Finally, it should be said that the duration of these experiments, in which the trauma was severe, suggests that the ability of the organism to survive may have been due to the suppression, by the anesthetic, of painful stimuli, permitting the available adjustment mechanisms to function to the fullest possible extent. This suggests the wisdom of the immediate administration of drugs to humans with severe burns to the point of effective and complete relief of all pain. It is suggested that even in patients in shock the inhibition of painful stimuli cannot but have the beneficial effect of permitting bodily adjustments to take place to an extent not possible when the vasomotor and cardiorespiratory systems are reacting strongly to noxious stimuli.

#### CONCLUSIONS

1. Changes occurring under continuous and adequate anesthesia in the circulating plasma, red cell and total blood volume, in blood oxygen and carbon dioxide content, in the hemodynamics, and in the blood electrolytes were followed in three nonsplenectomized and four splenectomized dogs which were subjected to thermal trauma.

2. The plasma volume was reduced immediately and markedly in all animals, due to a rapid loss of plasma fluid into the traumatized areas. Under further observation this loss continued, and a progressive increase in the insensible water loss brought about a continued reduction in the plasma volume.



3. Large increases in the total number of circulating red cells were effective in maintaining the total blood volume at a level adequate for the support of circulation and for meeting the oxygen requirement in the nonsplenectomized animals. In the splenectomized animals the total number of red cells was reduced and total blood volume was lowered progressively.

4. Arterial blood pressure paralleled the course of the total blood volume and, in three splenectomized animals, fatal circulatory collapse occurred when the systolic pressure had fallen to 50 to 70 mm. Hg, and the total blood volume had decreased about 35 per cent from initial levels.

5. Oxygen saturation of venous blood was reduced in all animals, reaching values of less than 10 per cent prior to peripheral collapse in those animals that succumbed.

6. A progressive uncompensated loss of body fluids and electrolytes may lead to the establishment of a vicious cycle of continued hemoconcentration, congestion, stasis, anoxia, hyperventilation, and acidosis, with eventual fatal respiratory and circulatory collapse.

7. The relation of the reactions observed in these animals to the rationale of the clinical treatment of severely burned humans is discussed.

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## PHAGEDENIC ULCER

### A REPORT OF THREE CASES

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IN 1909 Luckett<sup>22</sup> reported an unusual rapidly spreading ulcer of the abdominal wall. The patient, a gardener, noticed a small pimple on the skin of the left lower portion of his abdomen. He picked at this with his fingernail and on the following day observed that a scab covered the site of the former pimple. Removal of the scab revealed a small ulcer which spread rapidly. Six days after he had picked the pimple, the ulcer measured 2 by 3 inches. Twelve days later it measured 5¼ by 10¼ inches and had destroyed the skin covering the greater part of the lower abdomen. As a desperate measure, the entire ulcer, together with the skin well beyond the red area, was excised with the cautery. This treatment resulted in complete and rapid recovery.

Cullen<sup>11</sup> in 1924 described a "progressively enlarging ulcer of the abdominal wall involving the skin and fat, following drainage of an abdominal abscess apparently of appendiceal origin." In the same year Borelli<sup>5</sup> reported a case of "diffuse superficial gangrene of the abdominal wall after laparotomy" and Christopher<sup>9</sup> recorded his experiences with a "severe spreading carbuncular infection of the chest wall following rib resection." The older medical literature contains numerous accounts of enormous spreading ulcers of the skin, some of which are undoubtedly identical with these lesions, as has been pointed out by Bartlett<sup>4</sup> in her excellent review of the subject; but the interest of modern surgeons appears to date from the reports cited above.

Since 1924 descriptions of many closely allied lesions have appeared in the literature.<sup>1-3, 6-8, 10, 12-21, 23-29, 31-36</sup> The majority have occurred after drainage of an intra-abdominal abscess or an empyema. Some, however, have followed drainage of abscesses in other locations; i.e., the axilla, the groin, and the breast. A few are reported as having arisen from small cuts or scratches. Their rarity has made it difficult to study them and most workers have failed to realize that the cases in the literature, which are usually cited as examples of one disease, represent at least two clinical entities. Meleney has described two distinct types: one he calls progressive bacterial synergistic gangrene<sup>25, 26</sup> and the other chronic undermining nongangrenous burrowing ulcer.<sup>27-29</sup>

The first type, which usually follows the drainage of a peritoneal abscess or an empyema, is essentially a lesion of the skin. It consists of an outer red zone of skin within which is a purple zone. The skin on the central side of the purple zone is gangrenous and gradually liquefies, leaving an ulcer whose base is composed of dirty gray granulation tissue. The process spreads gradually but relentlessly, and unless it is checked by suitable treatment may denude the entire abdomen or back. From this ulcer Meleney has isolated two organisms;<sup>6, 25, 26</sup> a microaerophilic nonhemolytic streptococcus and a *Staphylococcus aureus*. The streptococcus is found in the spreading edge while the staphylococcus is said to be present in the more central gangrenous portions. The streptococcus is described as being "microaerophilic"; i.e., it is not an absolute anaerobe but prefers an environment that is at least partially anaerobic. When first isolated it may not grow aerobically at all, but after several transplants may become capable of aerobic growth. The staphylococcus is an aerobic hemolytic *Staphylococcus aureus*.

Chronic undermining nongangrenous burrowing ulcer is primarily a disease of the subcutaneous fat. The drainage tract of a deep or subcutaneous abscess fails to heal. The skin edges become undermined, roll in, and gradually die. Large areas of skin are undermined and destroyed, leaving an ulcer whose base is composed of pale granulation tissue and at whose margins the skin is often undermined for a distance of several inches. Deep sinuses form about large vessels in the axilla or groin and extend into the pelvis. The process also dissects about bones, such as the ribs and sacrum. From these lesions Meleney has isolated a microaerophilic hemolytic streptococcus.<sup>27, 29</sup> It shows the usual cultural characteristics of beta hemolytic streptococci but prefers an anaerobic environment and usually cannot be isolated unless anaerobic methods of cultivation are employed. However, in long-standing cases Meleney has recovered it on aerobic culture and the organism which he isolated anaerobically will grow aerobically after prolonged artificial cultivation.

Both of these lesions are extremely resistant to all ordinary methods of treatment and continue to spread in spite of many different sorts of local and constitutional therapy. It was soon learned, however, that excision of the skin and subcutaneous tissues down to the fascia well beyond the spreading margin of the ulcer would arrest the progress of the synergistic ulcers and permit healing to occur.

The chronic nongangrenous burrowing type also may be cured by complete excision, but the surgical problem is more difficult. The sinus tracts burrow under ribs, between muscles, and down about large blood vessels in such a manner that their surgical excision is exceedingly difficult and often dangerous. It has been necessary, therefore, to cast about for some other method of treatment. Holman<sup>17</sup>

treated several cases successfully with maggots. Meleney recently has advocated the use of zinc peroxide.<sup>27-30</sup> There are two pitfalls in this method of treatment which must be avoided:

1. All preparations of zinc peroxide are not effective, and one must be sure that he is employing zinc peroxide that is potent. A simple way of determining whether or not zinc peroxide is active has been reported by Meleney.<sup>30</sup>

2. Zinc peroxide cannot be expected to kill the bacteria if it cannot reach them. All sinuses must be widely opened and all overhanging edges of skin, undermined ribs, etc., must be cut away in order to obtain an effective application of the material.

In the past one and one-half years there have been two cases of chronic undermining nongangrenous burrowing ulcer in the wards of the New Haven Hospital. We have also treated a third case which cannot be definitely classified.

CASE 1.—C. K., a white male, 25 years of age, was admitted to the New Haven Hospital on Aug. 12, 1936. On March 16, 1934, while at work in a sand pit, he was struck on the right wrist by a stone. The skin was broken and some swelling appeared locally. One week later the original lesion had healed, but the glands in the right axilla became swollen, fluctuant, and tender.

On March 30, 1934, at the Charlotte Hungerford Hospital in Torrington, Conn., an axillary abscess was incised and drained. Instead of healing, the wound became larger and in spite of all sorts of local treatment an ulcer formed which gradually progressed over the thoracic wall. On Oct. 8, 1934, he was transferred to the Bridgeport Hospital. At this time he said the lesion in the axilla was "big enough to put your fist in." Three days after admission to the Bridgeport Hospital the patient's temperature rose to 106° and the lesion spread rapidly down the medial aspect of the arm as far as the elbow. Many methods of treatment were tried without avail and the lesion gradually spread over the thorax anteriorly and posteriorly. In spite of the extensive lesion the patient felt well and was up and about.

When he was admitted to the New Haven Hospital on Aug. 12, 1936, about two and one-half years after the onset of the disease, a large ulcer covered the entire medial aspect of the right arm, the axilla, and an area on the thorax extending from the level of the clavicle above to the tenth rib below and from the costal chondral junction anteriorly almost to the spine posteriorly (Fig. 1). The base of the ulcer was composed of dirty gray granulation tissue. At the edges in some places the skin was adherent to the base, while in others it was undermined for as much as six inches, the subcutaneous fat having been destroyed. In these areas the progressing border of the undermining process was marked by a raised red area which gradually faded off into normal skin. There were small sinus tracts in the axilla extending between the muscles and about the vessels. Motion at the elbow and wrist was normal, but the arm was fixed at the shoulder. Abduction to 20° could be obtained mostly through motion of the scapula.

During the period between Aug. 13 and Aug. 25, 1936, smears taken from the sinuses and from beneath the undermined skin showed gram-positive staphylococci and gram-negative bacilli. Aerobic and anaerobic blood agar plate cultures from the same areas were overgrown with *B. proteus*. Streptococci were seen in the cooked meat tubes but could not be isolated because of the presence of *B. proteus*. In an effort to eliminate *B. proteus*, sterile saline solution was injected through the skin in the red raised portion of the advancing margin. This was then aspirated and cultured. *Staphylococcus albus* was obtained.

On Aug. 26, 1936, under avertin and nitrous oxide anesthesia, the margins of the entire ulcer were excised with the Bovie electric knife. The excision was carried well beyond the red zone, and a dressing of zinc peroxide\* was applied according to the technique recommended by Meleney. Transfusions of citrated blood amounting to 1,800 c.c. were given during the immediate postoperative days.



Fig. 1.—Case 1, upon admission August, 1936. The incision in the skin of the back is in the advancing red margin of the lesion. It was made for bacteriologic purposes. The skin between it and the ulcer is all undermined.

Cultures were made from various portions of the excised tissue upon blood agar plates. These were incubated aerobically and anaerobically. Pieces of tissue were also incubated in tubes of cooked meat medium. From these cultures were isolated:

1. Diphtheroid bacilli
2. *B. proteus*
3. A nonhemolytic streptococcus forming large gray colonies and growing equally well aerobically and anaerobically on blood agar
4. A streptococcus which upon some occasions grew better anaerobically than aerobically; on blood agar plates, anaerobically, it formed a gray hemolytic colony; aerobically it formed a green colony with slight or no hemolysis
5. *B. pyocyaneus*
6. Hemolytic staphylococcus growing best aerobically
7. Unidentified gram-positive rods

Following the débridement, most of the ulcer tended to improve and the granulations became healthy. There was still some tendency to undermine the skin posteriorly near the spine. New sinus tracts formed in the axilla.

On Sept. 9, 1936, additional débridement was done in the axilla, consisting of excision of portions of the pectoralis major and minor muscles. At the same time a portion of the ulcer in the region of the spinous processes of the dorsal vertebrae was excised.

The zinc peroxide dressings were continued. On Sept. 12, 1936, it was noticed that a rib on the anterior chest wall was exposed. During the night of Sept. 23

\*The zinc peroxide was kindly furnished by the R and H Chemicals Department of the E. I. Du Pont de Nemours and Co., Inc.

there was a sudden severe hemorrhage from an intercostal artery. The undermined rib was removed, and the patient was given a transfusion of 500 c.c. of citrated blood on Sept. 30. Cultures taken from the tissue excised were overgrown with *B. proteus*.

Azoehloramid dressings were substituted at this time as the supply of zinc peroxide had been exhausted. Epithelium began to grow in from the margins posteriorly and inferiorly, but the granulations forming the base of the ulcer did not look healthy enough for grafting. After almost two months without improvement, pinch grafts were applied to several small areas as a test. These promptly disintegrated. On Dec. 4, 1936, there was a sudden rise of temperature and the right arm became swollen and tender. A few days later two sinus tracts which had tunneled down the arm were opened. By Dec. 14 a series of abscesses had formed on both the upper arm and forearm. These were opened and the thin gray pus which was obtained showed streptococci upon smear. Cultures revealed the organisms to be hemolytic streptococci capable of both aerobic and anaerobic growth, but growing more profusely anaerobically.



Fig. 2.—Case 1, June 1, 1937. There is still a small ulcerated area in the axilla.

From this time on the dressings were taken over by one person. They were done meticulously and zinc peroxide was resumed according to the technique recommended by Meleney. Only enough material was available to cover the arm and axilla so the remainder of the lesion was dressed with vaseline gauze. The entire lesion was cleaned daily by a profuse irrigation of physiologic saline solution.

By Dec. 23 the entire lesion was clean and on Jan. 4, 1937, pinch grafts were placed under the granulations over the entire back. Unfortunately zinc peroxide was not available and a vaseline gauze dressing was applied. The patient was given a transfusion of 600 c.c. of citrated blood following the operation. In spite of movement of the chest and the difficulty of preventing the patient from lying on the grafted area, most of the grafts took. Some of the grafts began to regress about Jan. 9, however, and Dr. Meleney, who saw the patient at this time, kindly made arrangements to procure enough zinc peroxide to cover the entire area daily.

The posterior aspect and the arm improved steadily. But on Feb. 2 an area of redness appeared over the sternum, and it was found necessary to excise the fifth, sixth, and seventh costal cartilages which had been undermined and honey-combed. The granulations did not seem to grow in any portion of the wound though the grafts grew slowly. On Feb. 15 the anterior surface of the ulcer was covered with small pinch grafts which were placed under the granulation tissue and the patient was given 500 c.c. of citrated blood. These grafts took fairly well. On Feb. 25 grafts were placed on the back where previous grafts had been lost. By this time the greater portion of the lesion was epithelialized, although there were a few nongranulating areas near the sternum where grafts would not take. On April 19, 1937, it became necessary to excise a small sinus tract together with a portion of a costal cartilage.

Fig. 3.



Fig. 4.



Fig. 3.—Case 1 (hematoxylin and eosin,  $\times 10$ ). Section through margin of ulcer showing destruction of subcutaneous fat with relatively normal epithelium and dermis above.

Fig. 4.—Case 1 (hematoxylin and eosin,  $\times 85$ ). Higher power taken through area indicated in Fig. 3 showing ulcer surface.

By June 1 (Fig. 2) the entire ulcer was healed except for a few small areas 1 to 2 cm. in diameter in the axilla. There seemed to be nothing to excise, and these were treated conservatively. Sometimes a small ulcer would appear in the



center of the old scar, only to disappear quickly. This state of affairs continued until Aug. 8, 1937, when it was decided to excise the area in the axilla. A long sinus tract was found extending high up into the axilla. This was laid wide open, but it healed very sluggishly, and it was not until Oct. 18, 1937, that the lesion was healed and the patient was discharged.

*Pathology.*—(Figs. 3 and 4.) Sections taken through the margins of the ulcer show that the lesion involves chiefly the subcutaneous fat. The epithelium and dermis are intact and free from cellular infiltration except at the periphery of the overhanging edge. The subcutaneous fat is absent beneath this overhanging edge of dermis and epithelium but as the lesion is followed toward the advancing margin this fatty layer gradually reappears. At first it is necrotic and densely infiltrated in



Fig. 5.—Case 2. The ulcer over the sacrum and perineum after débridement Sept. 16.

some zones with polymorphonuclear lymphocytes. As the border of the lesion is approached, the necrosis is absent, leaving merely a wall of inflammatory cells demarcating the limits of the process. The walls of the ulcer are lined by a layer of amorphous necrotic material which is heavily infiltrated with polymorphonuclear leucocytes. Beneath this is a zone of fresh granulation tissue composed of young fibroblasts and budding capillaries. Beyond this zone older granulation

tissue is seen. This is heavily infiltrated with lymphocytes, plasma cells, and rare polymorphonuclear leucocytes. The blood vessels throughout are intact and free from thrombi.

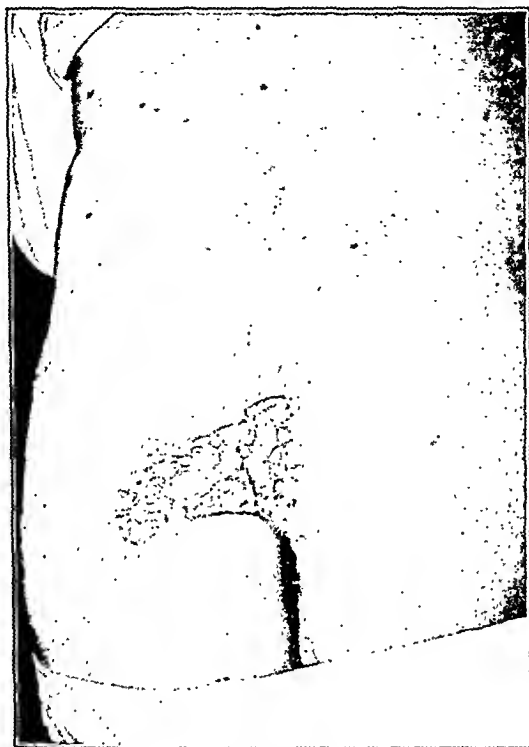


Fig. 6.—Case 2. The area shown in Fig. 5 after healing had occurred.

CASE 2.—E. M., a white male, 28 years of age, came to the New Haven Hospital Dispensary on Nov. 22, 1933, complaining of a sore in the right axilla. He stated that six weeks previously a red, tender lump had appeared in the axilla. The patient had applied hot compresses to the lesion, but, when this treatment failed, he squeezed the lump, forcing out a small amount of green pus. The lesion, failing to heal, continued to discharge purulent material. Examination revealed a sinus tract in the right axilla which extended beneath the skin for 3 cm. The entrance of the tract was surrounded by red indurated skin. The only other significant finding upon physical examination was a typical pilonidal sinus. The patient refused treatment that was offered and was not seen again until Oct. 16, 1935, when the skin of both axillae was thick, red, and perforated by the orifices of numerous sinus tracts. These could be traced for only short distances beneath the skin. The pilonidal sinus had become infected and it was possible to express pus from the many small orifices overlying the sacrum. Kahn and Frei tests were negative. An intracutaneous tuberculin test was positive. No cultures were reported. The patient again left the Dispensary and was not seen further until June 11, 1937, when he was admitted to the hospital. During the year and a half he had treated the axillary lesions with hot compresses and had succeeded in healing the one in the right axilla completely. The left axilla, however, was occupied by a larger ulcer whose base was composed of dirty gray granulation tissue. About the ulcer the skin was red and indurated but not undermined, and there seemed to be evidence of healing. The lesion, which

had started in the pilonidal sinus, had spread so that the perianal, lumbosacral, gluteal, perineal, and inguinal regions were occupied by a large ulcer, whose base was composed of dirty gray granulation tissue. The skin edges were undermined several inches in some areas, while in other places there were bridges of skin crossing the ulcer. Sinus tracts led down about the rectum, the sacrum, and dipped between the gluteal muscles.

Fig. 7.



Fig. 8.

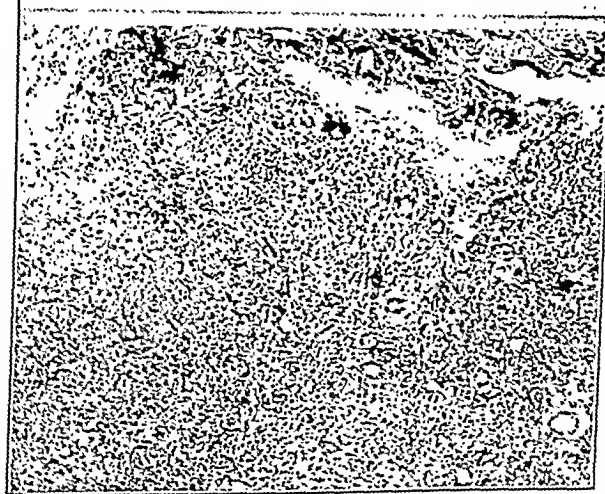


Fig. 7.—Case 2 (hematoxylin and eosin,  $\times 10$ ). Section through undermined portion of ulcer margin showing involvement of the subcutaneous fat with relatively normal epithelium and dermis above.

Fig. 8.—Case 2 (hematoxylin and eosin  $\times 125$ .) High power taken approximately through area indicated in Fig. 5 showing foreign body giant cells.

Aerobic and anaerobic cultures made on June 21 from the lesion in the left axilla and the ulcer over the sacrum were overgrown with *B. protus*. On June 22 more cultures were taken from many different locations in an effort to obtain some that might be free of *B. protus*. From these cultures were isolated:

1. Nonhemolytic anaerobic streptococcus
2. *Staphylococcus aureus*

3. Diphtheroid bacilli
4. *B. proteus*
5. Unidentified gram-positive bacilli (aerobic)
6. *Staphylococcus albus*

It did not seem that much etiologic significance could be attributed to such a heterogeneous collection of organisms. On June 29 a piece of tissue was excised from the margin of the ulcer. From the tissue nearest the ulcer were isolated diphtheroid bacilli, *Staphylococcus albus*, and anaerobic nonhemolytic streptococci, while from the tissue near the normal skin were isolated diphtheroid bacilli and *Staphylococcus albus*.

Treatment consisted of tub baths twice daily to keep the lesion clean. Injections of tartar emetic were given intravenously. There was very little change in the lesion over a period of two and one-half months, and on August 25 zinc peroxide dressings, according to the technique outlined by Melency,<sup>27</sup> were started. After two weeks of this regime, very little improvement was noticed. Therefore it was decided to excise the lesions radically. On Sept. 16 a wide excision of the ulcer in the lumbosacral area was done. The periosteum of the sacrum was exposed and a portion of the rectum lay almost free in the wound (Fig. 5). Zinc peroxide dressings were continued. Granulation tissue appeared in ten days.

On Oct. 19, 1937, the granulating area was covered with pinch grafts, nearly all of which took. By Nov. 29 the entire area was epithelialized. The left axilla had healed meanwhile, with no treatment other than the zinc peroxide dressing. Cultures taken Oct. 23 were overgrown with *B. proteus*.

The ulcer remaining in the perineal and inguinal region was removed on Dec. 2, following which the patient recovered completely (Fig. 6).

**Pathology.**—(Figs. 7 and 8.) Sections taken through the margins of the ulcer present an appearance identical with that of Case 1 except that the walls of the ulcer are lined by a thick layer of granulation tissue throughout which are scattered many multinucleated giant cells of the foreign body type. These are large cells with pale basophilic cytoplasm containing opaque bodies and with six to fifteen nuclei arranged in a ring about the periphery of the cell.

**CASE 3.**—L. G., a white male, 75 years of age, was first admitted to the New Haven Hospital on April 27, 1936. He had been well except for abdominal cramps and mild attacks of "indigestion" until ten months before admission to the hospital, when, following a severe attack of "indigestion," he began to lose weight and strength and to have a fever. Four months later a tender mass formed in the right flank and ruptured spontaneously, liberating a quart of pus. The sinus leading to the abscess cavity failed to close. A few months later he began to cough.

Upon admission the patient appeared chronically ill. There was a sinus tract in the right flank which could not be probed beyond 2 cm. but which was evidently longer. A large accumulation of fluid was noted within the right pleural cavity. When this was aspirated, thick green pus was obtained. A smear of the pus revealed a few gram-positive cocci in short chains. Hemolytic streptococcus, *Streptococcus viridans*, and *Staphylococcus albus* were recovered by aerobic culture. No anaerobic cultures were made.

A long series of operations ensued which included catheter drainage of the empyema, rib resection, and partial thoracoplasty in many stages with excision of portions of the parietal pleura in order to close the chronic empyema cavity. The sinus in the right flank failed to close and was explored. It ran down along the lateral abdominal wall to a large mass in the region of the cecum and was found to

connect with the appendiceal lumen. Due to the extent of the mass, it was necessary to resect the terminal ileum, cecum, ascending colon and to anastomose the ileum to the transverse colon. The cecum and appendix were occupied by numerous large papillomas which almost completely occluded their lumina.

The point of special interest here was the development of a spreading ulcer on the chest wall following one stage of the thoracoplasty.

On Nov. 26, 1936, about one month after operation and one week after discharge from the hospital, it was noted that one of the wound margins was being rapidly undermined. An ulcer 3 cm. in diameter formed during the next twenty-four hours, and the patient was admitted to the hospital. Aerobic and anaerobic cultures of pieces of tissue excised from the margins of the ulcer revealed hemolytic *Staphylo-*

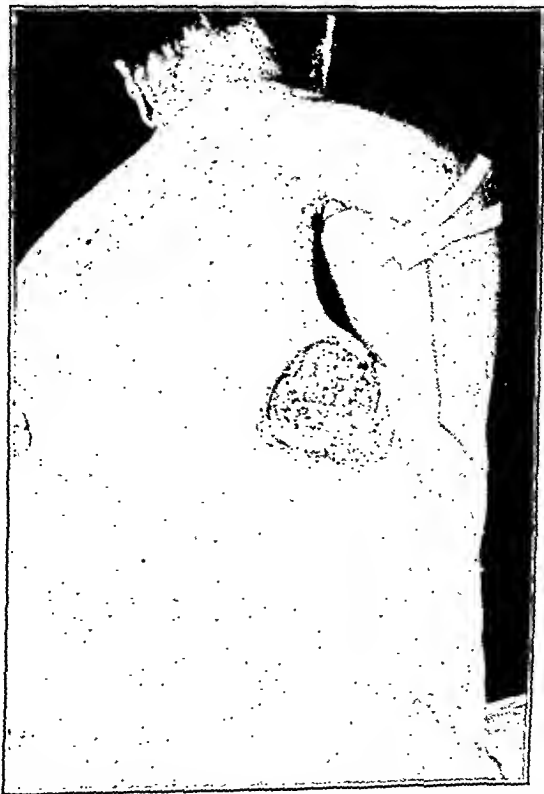


Fig. 9.—Case 3, May 30, 1937, just before the final débridement. Note the empyema cavity above the ulcer and the scars of the previous operations

*coccus aureus* and *Staphylococcus albus*. The margins of the wound were held open with adhesive tape and gauze saturated with  $H_2O_2$  was packed beneath them and changed hourly. The infection was readily controlled by these methods and on Dec. 14 the patient was discharged.

On April 22 a partial thoracoplasty was done and on May 10, 1937, he was discharged to be followed as an out-patient. He was readmitted because of the undermining of the margins at the lower end of the wound on May 24. Aerobic and anaerobic cultures of the ulcer margin at this time yielded diphtheroid bacilli and nonhemolytic streptococci growing equally well aerobically and anaerobically. It was hoped that this ulceration could be controlled as it had been previously by

merely excising the overhanging edges to get exposure and then packing the wound with gauze soaked in  $H_2O_2$ . In spite of this treatment, the ulcer spread. On May 28 under general anesthesia a wide resection of the ulcer was done with the Bovie cautery and continuous irrigations of hydrogen peroxide were started. Cultures of the excised tissue yielded the same organism plus *Staphylococcus albus*.

At this time the patient presented a residual empyema cavity with an ulcer 10 cm. in diameter at its inferior margin (Fig. 9). Its base was formed by fascia and its margins by the skin and subcutaneous fat. Laterally the margins were healthy but medially and inferiorly they were slightly undermined and the surrounding skin was raised and red for a distance of 2 cm. beyond the border of the ulcer. Zinc peroxide was applied according to Meleney's technique, but the under-



Fig. 10.—Case 3. The ulcer is completely healed, but there is still a small empyema cavity.

mining continued at such a rapid rate that one could note a change in three to four hours. Accordingly, under general anesthesia a really wide excision of the ulcer was done on May 30 and zinc peroxide was applied. Aerobic and anaerobic cultures of the excised tissue yielded the same organism as before plus *B. pyocyaneus* and *B. coli*, which were thought to be contaminating organisms acquired in the hospital.

The ulcer improved rapidly after the excision except in one area where the end of a rib was exposed. On June 22 pinch grafts were applied. The grafts took well and epithelium grew in rapidly from the margins.

By July 7 the ulcer was entirely healed except for a small sinus beneath the exposed rib. The rib was resected and thereafter the lesion healed completely. (Fig. 10.)

*Pathology.*—(Figs. 11 and 12.) Sections through the margin of the ulcer show a necrotizing process involving the epithelium, dermis, and subcutaneous fatty tissue. The edges are lined with necrotic tissue which is densely infiltrated with lymphocytes, plasma cells, and polymorphonuclear leucocytes. In zones where the ulcer has penetrated deeply into the subcutaneous tissues there is a marked tendency for

Fig. 11.



Fig. 12.

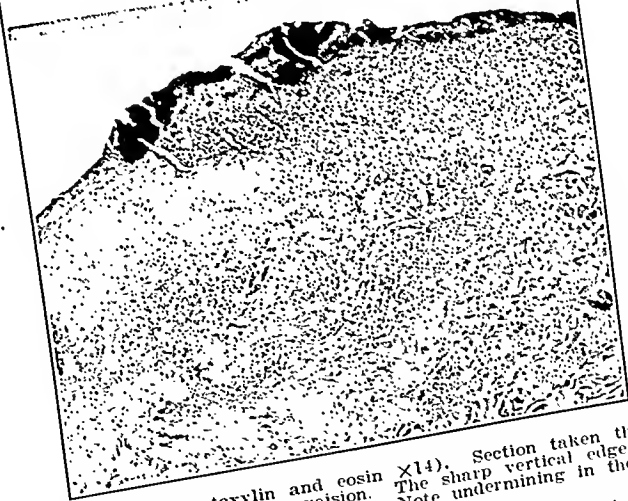


Fig. 11.—Case 3 (hematoxylin and eosin  $\times 14$ ). Section taken through margin of ulcer. Tissue removed at last excision. The sharp vertical edge of epithelium and dermis is due to previous débridement. Note undermining in the subcutaneous fat.

Fig. 12.—Case 3 (hematoxylin and eosin  $\times 85$ ). High power taken through one of the areas of skin necrosis. Note necrotic skin and cellular infiltration of dermis.

the cellular reaction to extend laterally, especially in the fatty layer. In the less penetrating portions the process appears to be confined chiefly to the subepithelial layers. The transition between normal and involved tissues is a gradual one with no wall of inflammatory cells demarcating the advancing margin.

The gross appearance and clinical courses of Cases 1 and 2 were quite similar. These cases, we believe, fall into the group of chronic undermining nongangrenous burrowing ulcers as described by Meleney.<sup>27</sup> The third case was entirely different clinically and seemed to resemble more closely the ulcers Meleney described under the title of progressive bacterial synergistic gangrene.<sup>25, 26</sup> Microscopically, however, except for a marked cellular reaction in the dermis just beneath the epithelium and occasional zones near the edge of the ulcer where the epithelium is necrotic, the picture is not unlike that seen in the first two cases. This ulcer was treated so early and its margins were excised so frequently that it did not have time to develop the typical clinical appearance of either type. For these reasons we are not willing to classify it definitely.

A review of the literature and our own limited experience has convinced us that Meleney's two clinical types of spreading ulcers and perhaps others exist. Whether these are bacteriologic entities in that they are each caused by specific organisms or whether they merely represent the reaction of certain patients to a nonspecific chronic infection, we are not prepared to say. Meleney, as pointed out above, has isolated organisms which he believes are the specific causative bacteria of each type of ulcer.

In the first two cases, which we regard as examples of the chronic undermining nongangrenous burrowing ulcer, the ulcers harbored *B. proteus*. This made all attempts to recover other organisms very difficult and may account for our failure to recover the organisms described by Meleney. In Case 1 streptococci were isolated in pure culture from an abscess when the lesion spread down the patient's arm and upon one occasion from tissue removed during a débridement. These resembled somewhat the microaerophilic hemolytic streptococcus described by Meleney. However, they were recovered from the ulcer proper upon only one occasion and certainly were not present in abundance. Furthermore they grew quite well aerobically.

In the third case we were not bothered with the proteus bacillus and in spite of repeated attempts we were unable to isolate a microaerophilic nonhemolytic streptococcus, or a microaerophilic hemolytic streptococcus.

The cultures described above were made by streaking 5 per cent rabbit's blood agar plates with material from the ulcer. Some plates were incubated aerobically and others anaerobically in a McIntosh-Fildes hydrogen jar. Portions of the tissue removed at operation were also incubated in deep tubes of cooked meat medium from which aerobic and anaerobic plates were made.

In an effort to establish the etiologic significance of the organisms that had been isolated, we attempted to reproduce the lesions in



animals. Numerous guinea pigs were injected subcutaneously with pure cultures and with various combinations of the organisms isolated from the ulcers.

In some cases we succeeded in producing necrosis of the skin which sloughed away leaving an ulcer with undermined edges, but these ulcers always healed promptly and never seemed to have more than a vague resemblance to the progressive spreading lesions in the patients. Furthermore we were able to produce similar ulcers in guinea pigs with mixed cultures obtained from patients whose wounds bore no resemblance to these spreading ulcers.

Some of the combinations of bacteria which produced ulcers in guinea pigs were injected subcutaneously into mice, rabbits, and a dog. The mice died promptly, but in the rabbits and in the dog abscesses formed at the site of injection, ruptured spontaneously, and healed. Pieces of tissue from the spreading margins of the ulcers of the patients were placed beneath the skin of guinea pigs. All of the pigs developed an indurated swelling at the site of the tissue which disappeared after a week or two without ever breaking down.

Holman<sup>17</sup> and Brumsting and others<sup>7</sup> report similar results with their animal experiments, in that they were able with some combinations of organisms to produce lesions in animals which, however, healed promptly. Holman injected into dogs a hemolytic streptococcus and a *Staphylococcus aureus* isolated from a case of chronic nongangrenous burrowing ulcer. He was able to produce a slough at the site of injection, but healing occurred rapidly, and the lesion did not resemble that seen in the patient. Meleney has not reported on any experimental inoculations with the microaerophilic hemolytic streptococcus isolated from the chronic undermining nongangrenous burrowing ulcers but Brewer and Meleney<sup>6</sup> reported the results of some animal inoculations with the organisms isolated from the progressive synergistic type of ulcer. They found that neither the *Staphylococcus aureus* nor the microaerophilic nonhemolytic streptococcus when injected subcutaneously in dogs, rabbits, and guinea pigs would produce a lesion but if they were injected simultaneously a necrotic area resulted which broke down and left an ulcer. In the guinea pigs and rabbits "the process generally reached its peak in three to four days and thereafter subsided. It did not spread progressively as in the human case." In the dog "on the fifth day frank gangrene developed at the injection site of the mixture and on the sixth day it sloughed out, leaving an undermined gangrenous margin. This spread slightly for a day or two and then subsided but showed very little tendency to heal."

#### SUMMARY

The three cases confirm the general experience of others in regard to the treatment of these ulcers. Ordinary methods of treatment are

usually of no avail and although these lesions, while under treatment, may tend to regress in one area while progressing in another or even regress and remain dormant for a time, they eventually will progress until they destroy the patient unless something radical is done. Before Meleney introduced the zinc peroxide treatment, there were only three or four cases reported in the literature that had recovered without radical excision of the ulcers.

In our three cases zinc peroxide alone was powerless to control the lesion, but, when used in conjunction with surgery, it seemed to be of definite benefit. It was never able to stop undermining of skin, ribs, or muscles alone but once these infected areas were completely removed, the material appeared to prevent recurrence. We have no proof of its mode of action and are unable to decide whether it acts specifically against anaerobic organisms by liberating oxygen, as Meleney believes,<sup>30</sup> or whether it merely provides a comfortable non-adherent dressing which promotes drainage and requires such meticulous care of the wound that healing results.

I wish to express my appreciation to Dr. Stanhope Bayne-Jones for his helpful suggestions, interest, and encouragement throughout the course of the work.

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## HYPOSPADIAS

### A DISCUSSION OF THE SUBJECT FROM THE VIEWPOINT OF RECONSTRUCTIVE SURGERY AND A REPORT OF THE USE OF A DEPILATED SCROTAL FLAP\*

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**H**YPOSPADIAS is a deformity of the male genitals, due to a failure of the embryonal completion of an essential structure, the urethra. The defect is always in the midline of the ventrum of the penis. One case varies from another only in the degree of developmental failure. The degree of the defect varies from a marking on the glans penis to a point where the sex of the individual may be questioned. It is important to note that both penile and serotal elements may be involved.

In the normal case the function of the urethra is that of a channel of evacuation of the urinary bladder and after puberty it plays an important role in the sex life of the individual.

The function of the scrotum is that of a covering of the testes. It is composed of epithelial structures which contain hair follicles which in this location do not produce until after puberty.

In the site and position of the absent structure appear firm, hard tissue, vestigial bands of the urethra, which inhibit complete erection of the penis and cause a condition called *enervature*.

Master surgeons have devoted their efforts to finding ways and means for the reconstruction of a part of the body which has been destroyed or rearranged by the invasion of disease, the application of force, or which has failed to develop congenitally or to grow normally. A splendid literature, discussed under the terms of reconstructive or plastic surgery, has developed and is accessible to any surgeon. Certain principles of procedure and requirements of success in the mobilization of tissue to repair a defect have been developed and generally accepted. The fundamental problem of repair of the deformity of hypospadias is to find tissue from somewhere to supplant the missing structures.

Thus I have analyzed the many operations suggested for the repair of hypospadias, studied the operative steps involved, tried to relate them to these principles and to sift out those steps which do not fit and concentrate upon those that do, in an effort to find the most reasonable solution of the question of method of reconstruction of the deformity.

1. *The Use of the Free Graft*.—The free graft, whatever its form, thin or thick, is severed from its original source of nourishment and transplanted to another part of the body. It is, therefore, potentially dead

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tissue and ideal situations must obtain for the development of new avenues of nourishment, however indirect, or complete or partial loss of the graft follows.

The successful transplant of a free graft depends upon: the use of one kind of tissue, a properly prepared base for its application, and fixation of the graft to the base by some agent of pressure.

In the repair of hypospadias the thin skin graft only has been used and thus the first requirement is readily met.

The preparation of the base of application in hypospadias is made by a trocar, around which the graft is sewn in reverse, being plunged into the body of the penis. The graft is thereby buried in a cleanly and newly prepared base, which meets the second requirement.



Fig. 1.—At the age of 7 years and 4 months, this boy was admitted to the hospital, in September, 1927, for the repair of hypospadias.

Pressure to produce fixation of the graft is exerted by the inflexible tube of the trocar placed within the soft movable tissues of the organ and its skin covering.

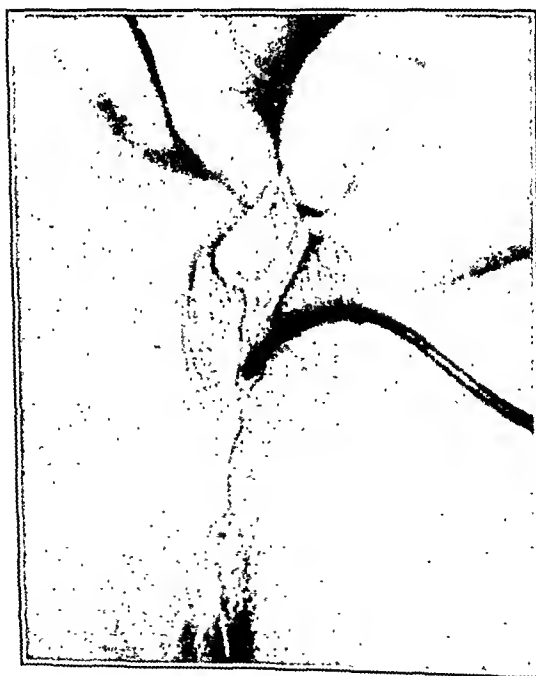
Experience has shown that success in free transplants is best assured where the graft is placed on structures which offer resistance to pressure. The tissues of the genitals are soft, pliable, movable and non-resistant and the possibility of exerting even firm pressure on the graft seems to me to be rather remote.

The use of the free graft in the repair of hypospadias was given a long trial at the beginning of the century by Nové-Josserand. Cecil

comments upon the persistence with which this plan has been followed in spite of inconclusive and varying results. The often demonstrated tendency of a free graft to contract when placed on soft movable tissue



A.



B.

Fig. 2. A. The close-up of the genitals. B. The opening is located at the rectotal-perineal junction. By the slightest depression of the tissues the catheter went straight in behind the pubis. First operation for the release of the penis was done, and the patient was discharged in a month.

requires the most meticulous care in after-treatment, to such a degree that the follow-up attention is as important, if not more so, than the actual performance of the operation. The tendency of the free graft to contract when placed on movable tissues renders its use in the immature patient with hypospadias questionable, because of the possibility, even probability, of encroachment of the penis increasing with future growth of the organ. In other words, the organ grows but the graft does not.

Recently McIndoe has responsored the plan, giving details of operative procedure and aftercare. His argument, however, seems to indicate that he is referring to the adult case of hypospadias, whether the operation be a primary procedure or one secondary to a partial or com-

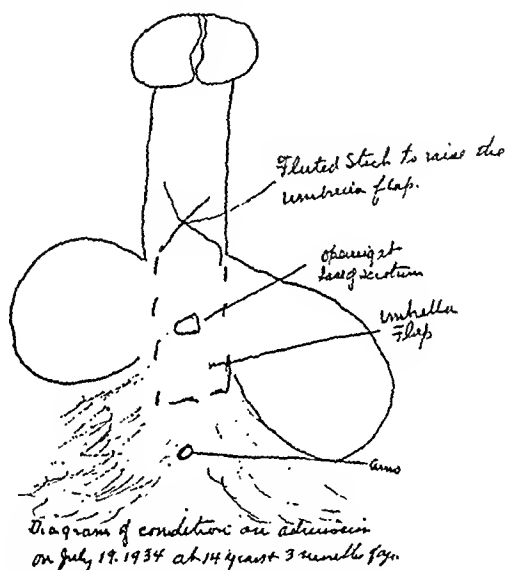


Fig. 3.—He was readmitted in July, 1934, a lapse of seven years since discharge. The penis was satisfactorily released, the opening relaxed also, requiring a channel to be built, the whole length of an approximately mature organ. Every plan of repair incurred a great risk of failure except the stepup operation of Gatewood. A pucker stitch was placed in the umbrella flap and the patient was discharged in eighteen days.

plete failure of a previous operation. The operation can be done but I believe should be attempted only with a full knowledge of the exacting precision required in the preparation of the graft, the possible technical difficulties of insertion and fixation, and the need for ultra-meticulous postoperative care.

2. *The Advancement of the Urethra.*—The rationale of the operation of advancement of the urethra is based on the fact that the urethra normally lengthens and shortens with the engorgement and recession of the cavernous bodies of the penis. In advancement of the urethra, the congenitally short urethra is placed in a forward position in the belief that it then will function normally in the new position. How-



Fig. 4.—He was readmitted in November, 1935, at the age of 15 years and 7 months. A photograph was taken on admission. The opening had been advanced to the penile-scrotal junction, was patulous, and the channel was filled by a tangled mat of black hair. The tissues were so elastic and pliable that it was possible to evert parts of the channel at a time. He was sent to the operating room without preparation and a tedious effort made to destroy the follicles with a fine fulgurating needle.

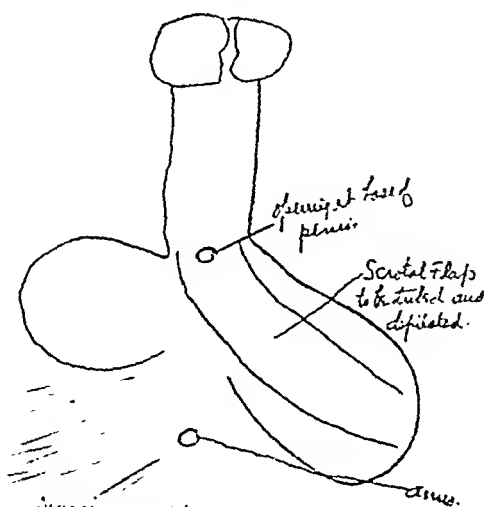


Diagram of condition on admission on November 21 1935 at 15 years and 7 months.

Fig. 5.—At the same operation, a flap was plotted on the scrotum, was positively tubed, and the hairs on it treated.



ever, in some cases it is difficult to determine the real length of the malformed urethra. The position of the opening is no index, because this opening itself shows many forms, even to a degree of almost complete stricture.



A.



B.

Fig. 6.—A, The picture of the form of the flap. Attention is called to the width of it. B, The picture of the puncture wounds. All healed without attention but objections to the method are discussed in the text.

In three weeks the flap was elongated one and one-quarter inches and further attempts to depilate were made, all under local anesthesia.

After school, in June, 1936, he was given another course of depilation and the distal end of the flap was incised, as a first step in its release.

I have positive evidence that the length of the urethra is also a cause for encurvature as well as the presence of the contractural bands distal to the opening. I have felt a deep responsibility in sending a boy out of the operating room with a more severe degree of hypospadias than that with which he entered it. I believe that the first operation for release of the penis is as important, if it is not the most important of all, as any of the operative steps, because the purpose of the repair is not only to build an intact urinary channel but also to construct a competent sexual organ.



A.



B.

Fig. 7.—In September, 1936, the flap was released, swung up, and attached to the right side of the penis by two series suture lines of removable stitches. A, Outside view of the flap; B, inside view of the flap; note a well-developed organ.

In the operation of mobilization the urethra is made into a single ended pedicle flap and the maintenance of blood supply in the flap must be fully considered. The degree of the deformity, therefore, must influence one in the selection of this plan, a plan necessarily limited to use in the lesser degrees of anterior penile and balanitic hypospadias, cases which I believe are questionable subjects for operation. I have been unable to make myself believe that a congenitally short urethra can be made to stretch the required distance without risk of causing an encurvature of the penis.

3. *The Transplant of Structures.*—If the principles of procedure and requirements for success in the use of flaps (*see* No. 5) and free graft transplants (*see* No. 1) are accepted, it must be concluded that success in the use of the appendix, ureter, vein, bladder mucosa, etc., for a new urethra results not from a technical victory but from a dispensation of providence.

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2. *The Surgically Tubed Flap Sutured in Reverse.*—The epithelium is on the inside of the tube.

A. Cut from the ventrum of the penis. Example: The inner tube flap of the Duplay-Thiersch operation, used by Blair-Brown, Cabot, etc.

B. Cut from the dorsum of the penis. Example: The Mayo operation.

C. Cut from the serotum. Example: The Lowsley-Begg operation.

3. *Sliding Flap.*—Example:

A. The outer flaps of the Duplay-Thiersch operation modified by Cecil into an overfolding flap, which, I believe, is based on the same surgical principle.



Fig. 8B.—See opposite page for legend.

4. *Pedicle Flaps.*—

*Single Ended:*

A. Cut from prepuce. Example: Edmunds, modified by Denis Browne into a recession flap. This flap was used in the 1870's by Van Horn.

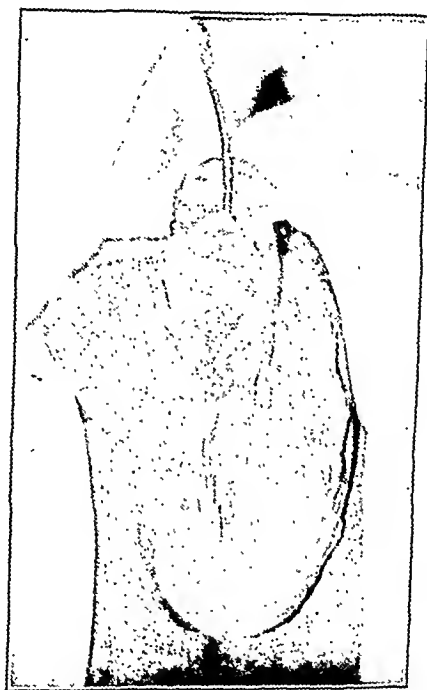
B. Cut from serotum. Example: Immediate transplant, Blair-Browne and Cabot. Delayed transplant, Bucknall.

C. Cut from penis and possibly serotum. Example: Ombredonne, popularized by Bevan and Gatewood as an umbrella flap, both of which are advanced flaps.

4. *Jump Flap From Outside the Genitals.*—This plan has never received attention.

When the amount of serotal tissue is considered, why should it be necessary to seek tissue from outside the genitals?

Because of so many questions of selection, possible technical difficulties, or, as in No. 3, when studied from the angle of tissue transplants, impossible procedures, I suggest that Nos. 1 through 4 be put aside and concentration of effort be made on No. 5.



A.

FIG. 8.—Following the transplant of the flap to the penis, he returned to school. In July, 1937, an incision was made on the left side of the penis, the flap split and fixed by two series suture lines, the inner line with hardened catgut, the other with removable stitches. The urine was diverted by a catheter which remained in position for ten days. There is an incompletely descended testicle on the right side. The flap was taken from the left scrotum. A, Side view; B, front view.

5. *Mobilization of the Tissues of the Genitals.*—The proposed operations include flaps cut from the prepuce, the epithelial envelope of the penis, and the scrotum.

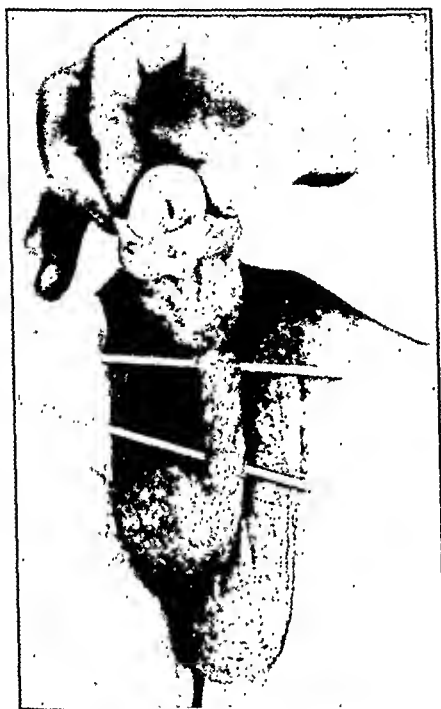
The flap operations have been known, have been discussed and rediscovered for many years by their sponsors. When these operations are broken down into separate technical steps, they are immediately resolved into different combinations of the use of several well-known forms of flap.

The forms may be tabulated as follows:

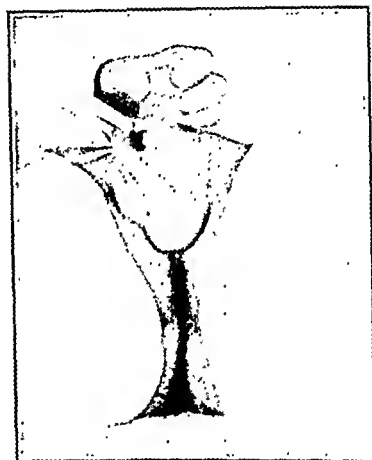
1. *The Surgically Tubed Flap Positively Sutured.*—The epithelium is on the outside of the flap. Example: The form shown in my illustrated case.

possibly in some of the muscle tendon transplants. But here there is no possibility of anticipating the frequency or degree of motion, due to the erectility of the penis.

It is impossible to anticipate the degree of postoperative edema. The scrotal tissues are more prone to swell after surgical attack than any other tissues of the body, except possibly the orbital tissues. Every surgeon will recognize that this factor has a very important bearing on the question of stitch tension.



A.



B.

Fig. 10.—The third case shows a midpenile hypospadias, a degree amenable to repair by the Duplay-Thiersch, Cecil, Browne combination. Had this been done in adolescent life, hair would have developed in the tube, because in this picture hair appears on the penile tissues up to the level of the opening. A, Note the profusion of hair on the flap and visualize the condition in any case wherein scrotal tissues are transplanted without preparation. B, The condition after six months of preparation. Compare this flap with the one shown in Fig. 6A. The flap in this case is too narrow and has given me some delay in release because of a coalescence of the puncture wounds at the base. The flap is viable and, although two fractional amputation incisions have been made, it has not caught up with its return blood supply. There is no reason to handicap oneself because of the wide spread of the tissues of the scrotum. The wider the plot, the longer the flap can be made at the first sitting.

There is limitation of the spread of the epithelial envelope of the penis. These unchangeable factors which make the avoidance of tension on suture lines so difficult doubtless explain the reason why the problem of repair of hypospadias apparently has been a great challenge over so many years.

My main difficulty in the repair of hypospadias has been in the limited spread of epithelial envelope of the penis in the operations, which

*Double ended:*

Example: Ombredonne cut from prepucce.

There are not so many forms but when cut from different areas of the genitals it is easy to look upon them as different procedures.

All flaps are acceptable and are wonderful contributions. It is still a marvel to me that we may attempt such operative procedures with any expectation of success. However, maintenance of blood supply, the avoidance of irritation during the process of healing, and complete release of tension of the flap and suture lines are necessary requirements for success with any flap, wherever cut or placed.

The genitals have an abundant blood supply. With ordinary care in the construction and placement of the flap, its life can be maintained even though flaps are cut in reverse to the channels of nourishment. Yet loss of tissue seems, according to the literature, to be a major consideration in replacing flap operations with other plans.

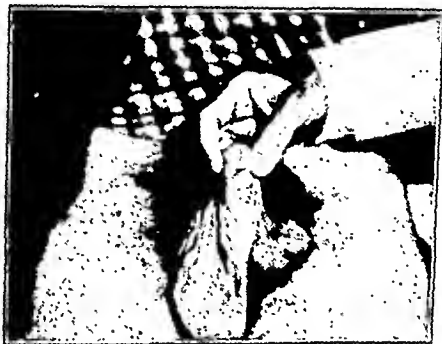


Fig. 9.—The picture of the condition on Nov. 2, 1938. A completely released organ, an intact urinary channel, and so far no complications. The flap has accommodated itself to a 14 F caliber channel. In this case the bladder cannot be entered by a flexible catheter, because a pouch was formed which lies ventrally and a little below the opening made by the umbrella flap. It is necessary that a rigid catheter, hugging the dorsal wall of the channel, be used. Note a balanitic hypospadias.

The avoidance of irritation in the process of healing is a general surgical principle in the care of any wound, but here it is most important because the whole effort of the operation is to construct an avenue of evacuation. Therefore it is necessary to divert the urinary stream by suprapubic, perineal, or catheter drainage.

The complete release of tension on flap and suture lines is another general surgical principle widely discussed in wound repair. In this situation this requirement is elevated to the peak of consideration, because several factors must be overcome to meet this requirement.

The parts cannot be immobilized. The genitals are appendages to the trunk and cannot be firmly sealed by dressings and support as is possible in other body areas.

The operation is done on a movable base. This same situation occurs in the soft palate, on the lip, and in the tissues about the orbit and

formation of a fistula. But is it not much more reasonable to attribute failure most often to tension on the suture lines, produced by erection, plus the tendency of these tissues to swell?

The difficulty I have had in the Duplay-Thiersch operation is in exactly plotting the tube flap. If the flap is made too generous, surely tension on the outside suture line follows. If it is made too narrow, it then becomes necessary to suture the thin margins of the flap in mere contact in an awkward position.

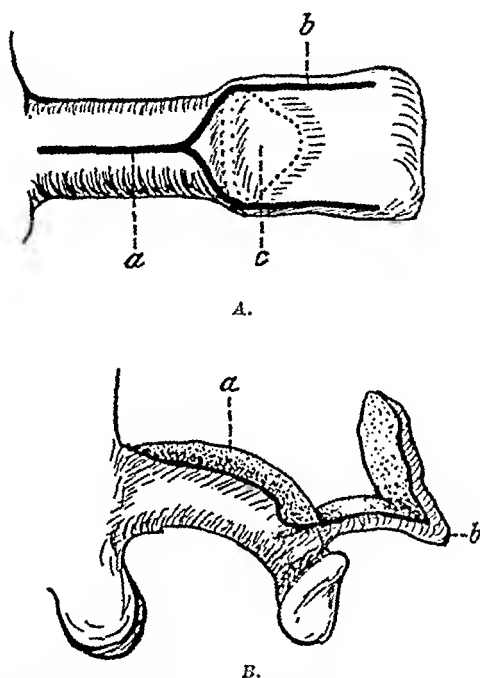


Fig. 12.—The plan of Browne to increase the spread of the epithelial envelope of the penis by receding a single-ended pedicle flap of the prepuce. Note that this flap is cut in reverse of the blood supply which comes from the base of the penis. A, The plot; B, the flap. (From Browne: *An Operation for Hypospadias*, *Lancet* 1: 141, 1936.)

Cecil modified the Duplay-Thiersch technique by a suggestion, in the cutting of flaps, of staggering the suture lines of the inner tube flap and the lateral sliding flap, the flaps being cut short on one side and long on the other (Fig. 11). From the viewpoint of tissue transplant, this procedure is a conversion of the flaps of the Duplay-Thiersch operation into overfolding flaps. I believe that these flaps are built on the same surgical principles, are splendid contributions and now generally accepted by all surgeons. I personally accept the Cecil modification as a milestone in the solution of the problem of repair of hypospadias.

The technique of Duplay-Thiersch and the Cecil modification do not take cognizance of what I believe is the most important requirement of success, sufficient tissue to meet stitch tension. It is to be observed that the covering of the penis lies loose when this organ is relaxed



I personally have accepted as the proper method of approach. In these operations there is a dearth of tissue to meet the question of stitch tension. On the contrary, with the use of the scrotal flap, a limitless supply of tissue is afforded and the problem of stitch tension is likely to be met with greater assurance of success.

Let us consider the penile flap and scrotal flap operations separately.

#### PENILE FLAP OPERATIONS

The need in operation for the repair of hypospadias is the construction of a tube in the position of a normal urethra and of the same length and caliber. The operation that best meets this requirement is a tube flap, cut from the ventrum of the penis, sutured in reverse,

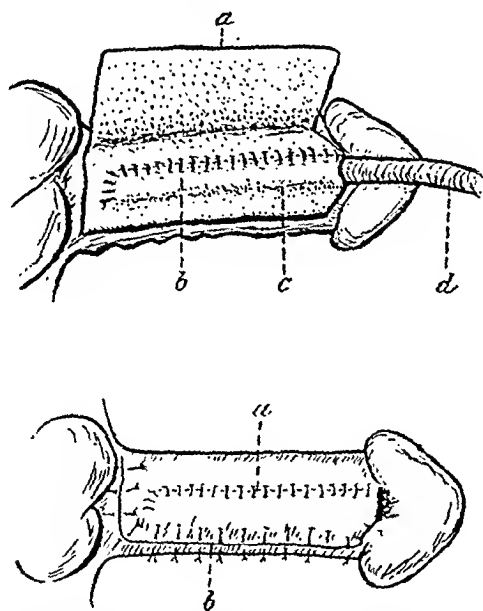


Fig. 11.—The Duplay-Thiersch-Cecil combination of flaps, the ideal operation for repair of penile hypospadias, to be done following the suggestion of Browne as shown in Fig. 12. (From Browne: *An Operation for Hypospadias*, *Lancet* 1: 141, 1936.)

and buried under the lateral sliding flaps, according to the now classical Duplay-Thiersch technique. If this operation were always successful, there would be no need for further consideration or discussion. Why has this method been put aside in favor of so many diverse methods? The reason is that not infrequently a fistula or fistulas or a complete breakdown of the suture lines have followed. The most frequent explanation of partial or complete failure is infection. Yet these tissues have a high degree of immunity and in more recent years there have been developed a number of very effective nonirritating antiseptics. Another explanation may be that unwittingly, in the suture of the tube flap, the needle has entered the channel, making an avenue for the

We have done this operation but once. Wallace Ritchie placed the flap with ease, with a perfect result, except for a spot of superficial necrosis along one of the suture lines, which healed readily. This flap is cut in reverse to the avenues of nourishment which come from the base of the penis. It requires care in preparation to meet the first requirement of flap transplants, maintenance of blood supply. By thus increasing the volume of the tissues of the envelope of the penis, a generous tube flap may be cut from the ventrum of the penis. Browne then suggests that this be sutured by the Connel intestinal stitch, which is, in effect, a continuous mattress, thus insuring a broad approximation of the denuded surfaces with a minimum danger of entering the channel by a stitch.

To illustrate this part of the paper, I have copied the illustrations of Denis Browne from his original article, because I believe that they illustrate by far the most reasonable combinations of flaps for the penile degree of hypospadias. Fundamentally, this is the Duplay-Thiersch operation, which purports to build a tube in the position of a normal urethra, plus the modification of Ceeil, plus the modification of Browne.

With this combination of flaps as a basis of study, discussions can now be directed to the problems of technical details, sequence of, and age for operation.

#### SCROTAL FLAP OPERATIONS

The handicap of insufficient tissue to assure release of stitch tension has been recognized by the plan of Ombredonne, the plan of Browne, and also the plan of Gatewood who by his stepup operation takes cognizance of the growth and accommodation of the tissues, and also by a technique widely used in the transplant of tissues, whereby successive operations are employed instead of the attempt being made to complete the operation at one sitting.

A fourth plan to meet the handicap of insufficient tissue is the use of scrotal tissues. The scrotal tissues are redundant, far beyond the actual normal requirement of covering for the testes, and no penalty is paid for their use. They are plastic, pliable, vital, and can be handled to meet all the essential requirements of flap transplant with more assurance of success than any other tissue in the body.

This fact has been recognized in a number of operations which invade the scrotum. To discuss or compare them in this paper would be no more than a repetition of what has been so beautifully done in the literature and more recently in a masterly way by Godard. However, for the sake of my argument, I selected for comment the Bucknall operation, offered in 1907.

When the scrotal flap operations are lined up for comparison, it is interesting to note that no matter how the operative steps differ the operations all have one procedure in common: *The penis is buried in the scrotum.*

and snug when erect. Although the penile tissues are very elastic, the expectation that they will meet on erection two different suture lines, on two different flaps, assumes a grave risk of failure.

The limitation of tissue in the penile flap operations has been long recognized by Ombredonne in an operation which increases the spread of the tissue on the ventrum of the penis by bringing the prepuce forward in the form of a double-ended pedicle flap. The Ombredonne operation yields a high percentage of successful results and has been supported by many critical surgeons. The reason for this success is the greater amount of tissue made available to meet the several factors inimical to release of tension of the stitches.

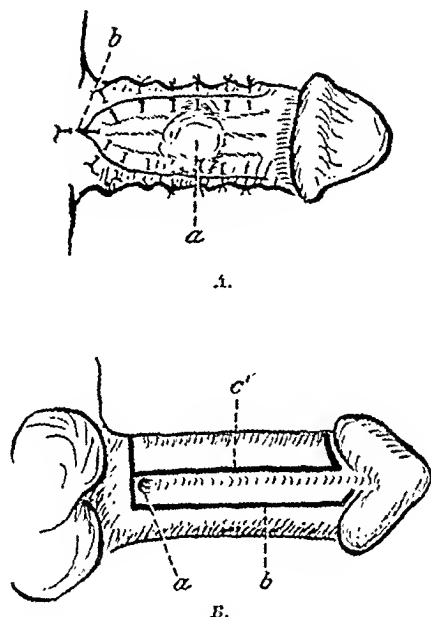


Fig. 13.—A, The flap placed on the dorsum of the penis, the Browne modification. B, The staggered incisions on the ventrum of the penis, the Cecil modification. (From Browne: *An Operation for Hypospadias*, *Lancet* 1: 141, 1936.)

Denis Browne now makes an original suggestion to overcome the handicap of insufficient tissue on the ventrum. The plan is original, not in the form of the flap but in its placement: This form of a single-ended pedicle flap is the oldest in surgery and is old in the repair of hypospadias, having been used as far back as the 1870's by Van Horn and in more recent years by Edmunds. It has been recommended in several modern contributions. But in all its previous usage, this flap was brought to the ventrum of the penis. Denis Browne places this flap on the dorsum. The situation can be described as a stem, around which is an epithelial envelope. The envelope is incised, the tissues mobilized to the ventrum, and then the defect is filled in by this flap cut from the prepuce (Fig. 12).

of the urethra. Thus two suture lines are buried and two exposed, four suture lines at one operation. Following a period of time to permit union, two more flaps, a right and left single-ended pedicle form, are cut wide of the suture lines to cover the released penis and the serotal flap. Keen surgical judgment is required to determine the time of release. The main objection to this operation is that the second principle of flap transplant is emphasized and the two operations require a diversion of the urinary stream for an indeterminate period of hospitalization. Even with such care, cases are reported with illustrations showing points of failure. While some of the serotal flaps recognize that the serotal tissues are hair-bearing after puberty, many do not.

(At this point of the argument, to avoid repetition, will the reader please scan the legends of Figs. 1 through 10, not only to criticize the technical details and sequence of procedure there shown, but to compare the operation with the Bucknall, each an example of the use of serotal tissues by two different methods of approach.)

When I saw hair growing in the channel following one of the steps in the repair of the case illustrated, I went over the literature again to find the status of the hair problem. It has been discussed from the beginning of the literature. I cannot find the exact reference, but the story is that some one suggested, when first the use of serotal flaps was offered, that it must be expected that, should the case live past puberty, a beard would appear at the meatus. The objection is not so exaggerated because to emphasize this phase of the subject I will say that in the illustration the mat of hair seen in the channel had the appearance of young beard.

Bucknall discussed the hair problem. He suggested that the penile flap be made wide and the serotal flap narrow, thus transplanting a minimum amount of serotal tissue. He also wondered whether the follicles would develop in their new position. Of course, they will, because the main requirement for success in flap transplant is live tissue.

I think everyone interested in these problems should read the article by Churchman, because he brings together the many failures following the repair of this deformity and it is startling to find all the things that may happen. He vigorously supports the Bucknall technique as following a proper surgical principle, but it is interesting to note that no mention is made of the hair problem.

Articles in the recent literature overlook this phase of the subject.

Every year I see cases reported where a serotal degree of hypospadias has been cured by the Ombredonne technique. I presume the reason for this lack of discussion of the hair problem is found in the present accepted ages for operation.

From the viewpoint of tissue transplants, this surgical step is now described as *carrying the deformity to the flap*.

I present a plan for the use of scrotal tissues based on the proposal to *prepare the flap and carry it to the deformity*.

The reason that the former plan has been always used in hypospadias is the fact that the penis when relaxed lies easily in contact with the scrotum and it is most reasonable to expect that this position would readily meet the question of stitch tension after the flaps are sutured.

In the Bucknall operation (Fig. 14) a flap is cut from the ventrum of the penis and sutured to a flap cut from the scrotum for the floor

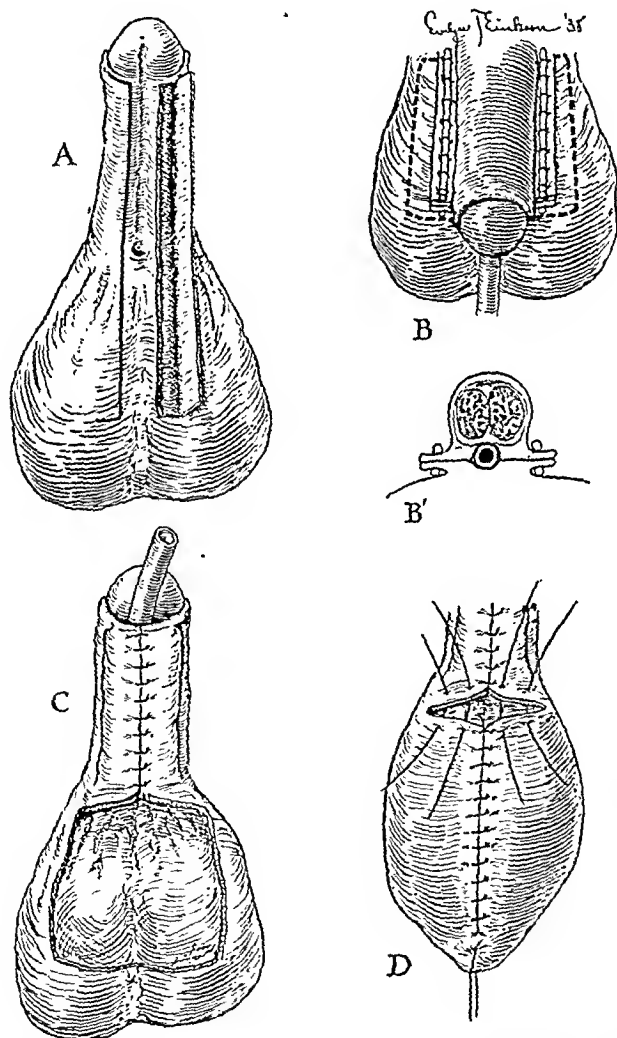


Fig. 14.—The Bucknall operation. It is here selected as an example of the use of scrotal tissue whereby the deformity is carried to the flap. It is to be compared with the plan for the use of scrotal tissue whereby the flap is prepared and carried to the deformity. (From Creevy: *Operative Treatment of Hypospadias*, *Surgery* 3: 726, 1938.)

This patient must be classed as a traumatic case, but the picture was identical with the penile-scrotal degree of hypospadias. The application of the procedure to the congenital deformity never crossed my mind, but when the problem arose, as shown in Fig. 4, I knew what to do.

The form of the flap is old in the literature but in recent years has been popularized by Gillies. It can be built to enormous lengths, providing the plot of it is properly made and the time element in its construction is correctly gauged. In this location, even in the most extreme case of perineal hypospadias, a flap can be made by encircling the scrotal tissue in different planes to fit the most extreme development of this organ. It is worth while to state that the flap remains rather rigid for an arbitrary period of three months, but gradually assumes the aspects of the normal scrotal tissues as shown in Fig. 7B.

I am uncertain as to the method for depilation. The objection to the fulguration needle is that it is difficult to control the area of destruction, with the possibility of coalescence and the formation of broad scar. This occurrence is of importance only at the base of the flap through which nourishment must come. The use of the x-ray as a depilatory agent is deprecated.

Possibly the treatment of depilation of the hair follicles can be better assured by excision. The hairs of the scrotum are discrete. When pulled by gentle traction, a white spot appears at the base. This can be anchored by a fine forceps and then clipped, which, of course, should be done in the long axis of the flap. Should a definite wound result, it may be stitched. Contiguous hairs can be taken care of at future sittings and thus overlapping wounds avoided. All of this may be done under local anesthesia without hospitalization.

It is to be noted (Fig. 9) that the end result in this case is a balanitic hypospadias. Is this sufficient? The literature so indicates and it was entirely satisfactory to my completed cases. However, should this result be unacceptable, the flap may be built long enough to extend beyond the glans.

I have wondered whether the flap so placed would withstand the traumatism of coitus. My first patient assured me that it would, but this is only one case. Possibly it would be better, in placing the flap, that a three instead of two series suture line be used. The fact is that with such a wealth of tissue available one may increase the spread of the covering of the penis to any degree selected.

In this case, because of my experience of a loss of a flap in my first case, I made a wide plot of the flap, thinking that at the second operation it could be cut to fit; but when the second line of sutures was made, the flap lay so evenly and easily without tension that it was used in toto. The result eighteen months later is that it has accommodated itself perfectly.

The general opinion is that the first operation for release of the penis from the contractural band may be done as a matter of convenience, depending upon the condition of the child. The requirement of this operation is that a complete release of encurvature is obtained.

The present idea is that hypospadias should be operated upon any time between the ages of 7 and 10 years, at least with a definite purpose to complete the case before puberty. At such an age there is no keen differentiation between the penile and scrotal tissues and, therefore, depending on the degree of the deformity, scrotal tissues may be included in the tube, whether penile or scrotal flaps are used.

In the reported case, I operated upon this patient at 14 years and 3 months of age, still appearing a boy. He returned to me at 15 years and 7 months of age, developed as a man. There is an occasional report of a case in which a hair ball has formed after puberty with deposit of lime salts, making what seems to me a serious complication at a time of life when this organ really begins to be of some use to the individual.

But these reports are few and far between, and from this experience I wonder if there are not a number of unreported cases of this complication. Is the formation of hair in the urethra of importance to the individual? Is it just as easy to take care of the hair formation after the operation? If so, what has been done? What is the relation of the hair question to the sex problem? These are questions I would like discussed, but they are, I believe, beyond the scope of my paper.

I would be less than frank were I to give the impression that the use of the scrotal tissue by this form flap and method of approach was developed through any initiative on my part. It was not, but it was used in my first case because of a peculiar set of circumstances.

#### CASE REPORT

A married man, 50 years of age, had lost, through some destructive inflammatory process some years previously, the whole urethra up to the penile-scrotal junction. The left cavernous body and one-half of the prepuce was the site of a hard, brawny scar. The hair question was not presented because the scrotal tissues were hairless, whether from the inflammatory process or long treatment, or both. I conceived the idea of building a tubed flap from both right and left scrotum and planned to swing them up on each side of the penis and sew them together. The left flap failed to meet the maintenance of blood supply in the flap transplant and an area of necrosis appeared in the midportion. During a period of uncertainty as to the next step, the right flap became flaccid, elastic, and evidently contained sufficient tissue to complete the repair. I brought it up first on the right side of the penis with catheter drainage of the bladder. In six months I completed by two series suture lines on the left side and in this instance diverted the urinary stream per perineal section. The result of these plans was most happy. The man assured me that I had constructed not only an intact urinary channel, but also a competent sexual organ.

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I am in no position vigorously to advocate the operation. I can say that there is no plan that I have used where I have been so free from concern during the process of healing. The patient voids, the parts are dried, protected by a diaper, the suture lines are exposed for care and observation, and the diversion of the urine required only for the last series suture lines. All of which is due to the fact that the quantity of tissue transplanted was sufficient to give not only a margin, but a wide margin, of safety, to meet the several factors inimical to stitch tension peculiar to this part of the body.

### CONCLUSIONS

1. The crux of the problem of repair of hypospadias is to find sufficient tissue to guarantee release of tension on the suture lines.
2. A revision should be made of the questions of age for operation in order to meet the hair question.
3. The literature should be sifted of several procedures, which evidently were once suggested on the idea that something special should be attempted to repair the deformity.
4. The problem of repair of hypospadias should be approached from the viewpoint of tissue transplants, because the operative steps involved are familiar to every surgeon and have been discussed from the dawn of medical history.
5. The tissues used in the repair should be those of the genitals, because they are native to the parts and thus have the potentiality of future growth and accommodation in the new position.

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scent. To avoid confusion, the terms maldescent or imperfect descent will be used to include all variations from the normal descent of the testis. The term ectopic testis will be used to mean a testicle that has descended into an abnormal position away from the course taken by the normal testis as it descends into the scrotum.

Although in rare instances perineal testis has been reported to occur as the result of trauma,<sup>1</sup> we are concerned in this discussion only with the anomaly of congenital perineal testis. The condition is not common. Altogether there have been recorded somewhat over 100 cases in the literature. Perineal testis was first described by John Hunter<sup>11</sup> in 1786, when he reported 2 cases. The first detailed account of the anomaly, however, was given in 1857 by Curling,<sup>7</sup> who collected 9 cases. In 1879 Annandale performed the first successful operative



Fig. 1.—Case of undescended perineal testis. Photograph taken between the first and second stages of the Torek operation. Note just behind the right scrotum the labium-like fold of skin which contained the ectopic processus vaginalis and gubernaculum.

cure of a case of perineal testis.<sup>5</sup> By 1889 the reports of 30 cases had been collected by Monard and Terrillon.<sup>16</sup> In 1899 Weinberger<sup>21</sup> collected 74 cases, and in 1906 Klein<sup>13</sup> assembled 81.

In 1857 Godard<sup>10</sup> found 3 cases of perineal testis in a series of 53 cases of maldescended testis studied by him. In 1903 Eccles<sup>9</sup> found only 5 cases among 936 cases of imperfectly descended testis associated with hernia. W. B. Coley<sup>3</sup> says that from 1890 to 1907 at the Hospital for the Ruptured and Crippled there were 737 cases of maldescended testis associated with hernia and that in only 15 instances was a testis found in the perineum. All but 6 of the 737 cases came to operation. One hundred twenty-six of the cases were operated upon by Coley himself and 9 of these had a perineal testis. Burdick and B. L. Coley<sup>3</sup> report 537 operations for maldescended testis on 482 patients at the Hospital for the Ruptured and Crippled from 1891 to

# UNDESCENDED PERINEAL TESTIS

## REPORT OF A CASE

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**E**CTOPIA testis is an unusual condition and ectopia testis perinei is therefore still more uncommon. "Potential" perineal testis, i.e., an undescended inguinal testicle associated with the anatomic features of perineal testis, is apparently rare. For that reason the following case is reported.

### CASE REPORT

D. C. (University of Virginia Hospital No. 128889), a 13-year-old white boy, was admitted to the hospital on July 12, 1938, because of an undescended right testicle. An older brother had been operated upon for the same condition in 1932.

Examination revealed a well-developed boy with no testicle in the right scrotum. The penis was mature and the left testicle was somewhat larger than the average. The right half of the scrotum was small and its lateral attachment was closer to the midline than usual. Lateral to the right half of the scrotum and separated from it by a deep groove there was found an anomalous, labium-like fold of skin that extended from the region of the pubic spine to a point well down in the perineum (Fig. 1). Within the fold there was felt a linear structure thought to be the ductus deferens. The superficial inguinal ring on the right side was small and was identified with difficulty. In the position of the inguinal canal on the right there could be felt a rounded body that was approximately 1.5 cm. in diameter. There was an indirect inguinal hernia on the left side.

On July 13, 1938, a left inguinal herniorrhaphy was first done by the Ferguson method. The right inguinal canal was then opened and the processus vaginalis, a large sac communicating with the abdominal cavity, was immediately encountered. Projecting into the posterior wall of the sac was the right testicle, epididymis, and ductus deferens. The peritoneal sac extended downwards over the pubis into the labium-like fold in the perineum described above. Also extending into the fold was a loop of the ductus deferens and the gubernaculum testis. The latter was a well-developed structure whose proximal end was attached to the lower pole of the testis and whose distal end was firmly fixed to the bottom of the anomalous perineal fold.

The peritoneal sac was transfixed and ligated at a high level and amputated. The lower portion was then freed from the testicle and the structures of the cord and dissected out of the perineal fold. A finger was thrust into the right scrotum and a channel was easily burrowed out beneath the superficial fascia. There seemed to be a natural point of lessened resistance through which the finger passed. The gubernaculum was cut at its insertion in the perineal fold. The spermatic cord was of adequate length, and a typical Torek procedure was carried out without division of fascial bands or vessels.

### PERINEAL TESTIS

There was found upon reviewing the literature some variation in the terminology used in referring to abnormalities of testicular de-

At the beginning of the third fetal month an evagination of the peritoneum takes place at the site of the future abdominal inguinal ring to form a saclike pouch, the processus vaginalis. This peritoneal process passes through the inguinal canal and over the pubis into the scrotum.

By the end of the third month the early degeneration of its cranial portion associated with a more rapid elongation of the trunk has produced a relative descent of the testis, so that it occupies a position at the boundary between the abdomen and the pelvis near the future abdominal inguinal ring. There is little further change in the position of the testis until the beginning of the seventh month, when the gubernaculum has ceased growing and has begun to shorten. Most anatomists believe that the further descent of the testis is brought about fundamentally by a traction force of the gubernaculum. The testis is pulled into the inguinal canal dorsal to the vaginal process of peritoneum. During this period the gubernaculum shortens by one-half. The gubernaculum continues its process of shortening and the testicle passes out through the superficial inguinal ring and finally reaches the scrotum, usually about the end of the ninth lunar month, or shortly before birth. In the newborn male the gubernaculum is only about a quarter of its original length. The proximal part of the processus vaginalis becomes obliterated just before or soon after birth, while the distal part persists as the tunica vaginalis testis.

While the degeneration of the cranial portion of the early gonad, the disproportionate growth of the trunk as compared to that of the genital gland, and the traction force of the gubernaculum are at present considered to be the main factors in the production of the descent of the testis, there are other forces which probably play a part to a greater or lesser degree. Intra-abdominal pressure, resulting from the growth and enlargement of the viscera of the abdominal cavity, probably helps to force the testicle into the inguinal canal in much the same manner that an inguinal hernia is formed. Active contraction of the abdominal musculature undoubtedly aids the testicle in its passage through the inguinal canal.

#### ETIOLOGY OF ECTOPIC TESTIS

In reports of cases of congenital ectopic testis there are numerous theories offered in explanation of the ectopia, many of which center on the gubernaculum.

A once popular gubernacular theory for the explanation of ectopic testis in general was advanced by Lockwood<sup>14</sup> in 1887. Lockwood thought of the gubernaculum as a structure with multitailed insertions. He considered one strand to go to the scrotum, one to the root of the penis, another to the perineum, another to the pubis in the region of the superficial inguinal ring, and finally one to the femoral

1924. In this group there were 86 cases of ectopic testis, but not one of these was of the perineal type. Campbell<sup>4</sup> states that there was no case of perineal testis found among 36,000 urological admissions at Bellevue Hospital.

#### NORMAL DESCENT OF THE TESTIS

The details of the mechanism by which the testis normally becomes transferred from its position of origin on the dorsal abdominal wall to its final location in the scrotum are not entirely understood. During the fourth week of fetal life, the mesonephros begins to develop from the nephrogenic cord or unsegmented intermediate mesoderm in the dorsal portion of the embryo. Growth of the mesonephros causes it to bulge ventrally into the coelomic cavity, where it is known as the urogenital fold. Cranialward the urogenital folds of the two sides are separate, but caudally they fuse together to form the genital cord. The coelomic epithelium on the ventromedial surface of the urogenital fold becomes thickened and many layered, so that by the sixth week it is bulging independently into the coelom as a longitudinal fold, known as the genital fold, which is the primordium of the gonad. The genital fold increases in thickness and becomes constricted away from the mesonephros by deepening medial and lateral grooves. These grooves remain separated from each other by a thin attachment or mesentery which, in the case of the testis, is later to become the mesorchium. As development of the genital gland continues, the more cranial segments of the primordium degenerate so that it becomes shortened and more compact. The degenerating cephalic segments persist for a time as the diaphragmatic ligament which is attached to the cranial pole of the gonad.

Toward the end of the second month the component parts of the gubernaculum develop. The most caudal portion of the genital fold becomes fibromuscular and attaches the testis to the genital cord. It is known as the ligamentum testis. About the seventh week of fetal life there appears an inguinal fold that extends between the genital fold and a prominence on the anterior abdominal wall, called the inguinal crest. Within the inguinal fold there is developed a fibromuscular band called the chorda gubernaculi. The abdominal musculature becomes developed around the chorda to form the inguinal canal. At its distal end the chorda gubernaculi becomes connected to another band, the ligamentum scroti, which extends to the scrotal swelling and later to the bottom of the scrotal pouch. Now by condensation to form a fibrous cord within the genital cord, the proximal end of the chorda gubernaculi becomes united to the distal end of the ligamentum testis, thus effecting a continuous ligamentous structure, the gubernaculum, which extends all the way from the caudal pole of the testis to the scrotal swelling.

or sac is a striking part of the picture" in both perineal and penile positions of the testis. Describing his case of perineal testis, Robertson<sup>17</sup> speaks of a pocket in the perineum in which the testicle lay, being attached there by a gubernaculum 3 mm. in diameter. Pulling on this fibrous band, he says, would cause a dimpling of the skin of the perineum. Eccles<sup>8</sup> also speaks of an adventitious sac, in cases of perineal testis associated with hernia, that lies lateral to and is separated by a sulcus from an imperfectly developed scrotum.

The present case presents an interesting element of heredity in that the patient's brother had an operation for undescended testis at this hospital in 1932. In the brother's case the left testicle was found in the inguinal canal and the processus vaginalis had not descended beyond the testicle.

It is believed that this rare case offers some evidence bearing on the unsettled problems of abnormal descent of the testis. Sommeland<sup>18</sup> says: "Congenital perineal testis is often accompanied by some abnormality of the corresponding vaginal process of peritoneum. No instance is known in which the vaginal process found its way into the scrotum while the testis went into the perineum. Since under normal conditions the vaginal process precedes the testis into the scrotum, it probably precedes the testis into the aberrant position in these abnormal cases." Sommeland's prediction is fulfilled in this case. It is evident, therefore, that there must be some common factor that is responsible for the combined aberration of both the processus vaginalis and the testicle in cases of perineal ectopia; otherwise both of these structures would not always be ectopic at the same time. Inasmuch as the processus vaginalis precedes the testicle in its descent, it might at first appear that the primary aberration is one of the processus vaginalis. However, when we consider that the gubernaculum is developed somewhat ahead of the descent of the processus and that the former does not descend but is developed in situ, so to speak, from three sources, it is difficult to see how the processus vaginalis could influence the position of the gubernaculum and, hence, the final position of the testicle.

The cause of the descent of the processus vaginalis and its direction normally into the scrotum is obscure. The peritoneal process probably originates as a result of increasing intra-abdominal pressure and is directed into the inguinal canal by the abdominal inguinal ring. It may be assisted through the canal by the contraction of the surrounding musculature, but after its emergence from the superficial inguinal ring there is no ligamentous structure present to pull or guide the processus into the scrotum. How it gets there is purely a matter of speculation. It may be that there is a plane of reduced tissue density that extends to the scrotum; or the gubernaculum, which lies posterior to the processus, may act as a growth-stimulating focus along which

triangle. Lockwood, therefore, explained ectopic testis upon the basis of overdevelopment of a gubernacular strand attached in an ectopic region. This theory in recent times has been largely discarded.

Others, notably Sonneland,<sup>18</sup> think that ectopic testis is mainly contingent upon an insufficiency or rupture of the gubernaculum, which, in certain cases, may become reinserted in an abnormal location. Still others ascribe the cause of *ectopia* to a primarily abnormal insertion of the gubernaculum. Burdick and Coley<sup>3</sup> believe that certain types of ectopia are due to rupture of the gubernaculum and that other types, including perineal ectopia, are the result of an abnormal gubernacular insertion. Congenital insufficiency of the length of the spermatic cord is another explanation that has been offered.

Next in frequency are the obstructive theories of ectopic testis. These theories all assume some mechanical means by which the testicle is obstructed in its descent or pushed from its normal course. McGregor,<sup>15</sup> in a careful study of the fascial planes of the anterior abdominal wall and perineum, describes various congenital fascial pockets and fascial ridges that, when present and well developed, may interrupt or deflect the testicle in its descent. Other mechanical explanations for ectopia include such conditions as fat plugging the scrotum, hernia pushing the testis from its course, and adhesions developing between the testis and the neighboring tissues.

Uffreduzzi<sup>20</sup> considers heredity a very important element in the production of ectopic testis. The heredity theory was first advanced in 1857 by Godard,<sup>10</sup> who reported a case in which both a father and son had a perineal testicle. In twenty-four cases of ectopic testis examined by Uffreduzzi, other anomalies were found in each. Uffreduzzi claims that degenerative signs can be found in the great majority of the cases of ectopic testis.

#### COMMENT

The chief significance of the case here reported lies in the fact that both the gubernaculum testis and the processus vaginalis extended into a fascial pocket in the perineum. If the gubernaculum is the principal force that governs the descent of the testicle following its emergence from the inguinal canal—and this is the prevailing opinion—then it seems reasonably safe to say that if the patient's testicle had descended it would have descended into the perineum. Hence, it should be considered a "potential" or an "undescended" perineal testicle.

Coley<sup>6</sup> refers to this type of case when he states that in some cases of inguinal retention of the testis the processus vaginalis may extend beyond the inguinal canal to the scrotum but occasionally may miss the scrotum and pass into the perineum.

A perineal fold or pouch is not, apparently, an uncommon finding in cases of perineal testis. According to Sonneland<sup>18</sup> "a fascial pocket

## SUBCUTANEOUS DORSAL DIGITAL BURSTITIS

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**S**UBCUTANEOUS adventitial bursae are known to occur about the bony prominences of most of the major joints of the body. Those of most frequent recognition when traumatized or diseased are the prepatellar and olecranon bursae. The dorsal digital bursae of the fingers are subject to disease with almost as great a frequency and may be the cause of continuing disability or prolonged medical treatment if they are unrecognized as the primary source of continued pathologic change in the finger.

Spalteholz<sup>1</sup> pictures and describes these small bursae lying between the skin and the extensor tendons on the dorsum of the finger joints as follows:

1. "Dorsal Digital Subcutaneous Bursae. Immediately beneath the skin, on the dorsal surface of the digital articulations, usually small and are fairly constant over the first interphalangeal joints, occasionally occur over the distal interphalangeal joints."

2. "Dorsal metacarpophalangeal bursae occasionally occur on the dorsal surface of the metacarpophalangeal articulations, and then usually only on the 5th finger."

3. "Inter-metacarpophalangeal bursae, of frequent occurrence, from one to three in number. Small, and lying between two neighboring fingers, at the metacarpal heads dorsal to the transverse capitular ligaments, between the second and 5th fingers."

A particularly good illustration in Toldt<sup>2</sup> shows these bursae clearly.

In 1933 a minor finger wound on the dorsum of the index interphalangeal joint under treatment in the office healed, broke down and drained, healed, then drained repeatedly. A foreign body, bone, or joint infection could not be made out. A glance at the illustration of Spalteholz brought out forcibly certain points in the anatomy, forgotten since student days. When the roof of the previously unrecognized bursa was removed, allowing complete drainage, prompt and lasting healing occurred. This first case was under treatment for fifty days. Since then, twenty-six further cases of digital bursitis have been recognized in office patients.

The usual history is that, following a cut, abrasion, or scratch on the dorsum of one of the finger joints, the small wound heals. A latent period of from three to twenty days is followed by increasing soreness of the joint, swelling, redness, and tenderness. The wound may reopen and drain pus or the inflamed bursa may rupture and



the cells of the peritoneal pouch grow toward the scrotal sac. The gubernaculum cannot directly pull the processus vaginalis into the scrotum, because at this stage the two structures are not adherent. Furthermore, the gubernaculum does not begin to shorten until after the processus has reached the scrotum. Should the ligamentum scroti portion of the gubernaculum be developed in an abnormal position, lateral to the scrotum with its distal attachment in the perineum—possibly in the bottom of a supernumerary scrotal pouch—it is conceivable that the gubernaculum might mechanically block the passage of the processus vaginalis into the scrotum and deflect it also into the perineum. Such a mechanism could readily explain the combined aberration of both gubernaculum and processus vaginalis that occurred in the case here reported and may possibly be the etiologic basis of perineal testis. The anatomic characters of the present case, i.e., the fully developed perineal processus vaginalis and gubernaculum, together with the inguinal position of the testicle, offer evidence that a common cause has deflected the entire direction of development. Whether or not the primary element behind this deflection lies with an abnormal gubernacular origin must remain a matter of speculation.

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intermetacarpal phalangeal bursae. Intermetacarpal phalangeal bursitis is recognized by pain on lateral compression of the metacarpal heads and the depth of the drainage, signs of true purulent arthritis being absent. Proximal interphalangeal or midjoint bursitis occurred in 9 instances, and the bursae over the distal phalangeal joint were inflamed in 5 cases. It is evident that the metacarpophalangeal joints suffer trauma more frequently. The individual fingers show the following frequency of bursitis; mid- or third fingers, 12 cases; index finger, 9 cases; fifth finger, 3 cases; ring finger, 2 cases; thumb, 1 case. Spreading cellulitis was a complication in 5 cases.

Acute traumatic hemorrhagic bursitis was observed in 2 patients following blunt nonpenetrating trauma. Splinting the affected finger for a week proved effective, nondisabling treatment. One instance of chronic metacarpophalangeal bursitis was observed on the midfinger knuckle of a file clerk who pushed back heavy files with the dorsum of the affected hand.

In 21 patients the bursitis was recognized early in the course of treatment. These patients averaged 13.4 days of treatment and 2.1 days of disability. Two patients with acute cellulitis are included in this first group and were disabled 17 and 23 days respectively. Six patients received treatment from other physicians before coming to the office or were seen in consultation. An average of 74 days had elapsed before the bursitis was recognized. This second group averaged 44.1 days away from work. The average time necessary for permanent healing after unroofing the bursae was 22 days. The average total time of these patients under a physician's care was 92 days. Such cases are probably the source of medical and folk lore, concerning poor healing over the knuckles. "The wound keeps breaking open." Keep it open and it heals more quickly.

From 1933 to 1938, 22 cases of acute subdeltoid bursitis (peritendinitis calcificans), 27 instances of traumatic prepatellar bursitis, and 20 cases of acute olecranon bursitis were seen in office patients. The relative frequency of digital bursitis, and the patient's economic loss, the prolonged treatment of insignificant wounds, when such bursae are unrecognized, call for more vigilance in the treatment of minor finger injuries.

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drain beside the healed scar. With rupture, relief of symptoms lasts only a few days. Healing, reappearance of inflammatory signs occur, and the cycle is repeated. With added new trauma, local cellulitis, lymphangitis, and adenitis may appear. The bursitis is recognized by swelling of the dorsal surface of the joint, tenderness only on the dorsum, not on the lateral or palmar surfaces, and pain on flexion which limits the motion of the finger. If one unroofs the bursa with a sharp scalpel, leaving only the floor and shallow walls, prompt healing takes place (Fig. 1). In cases recognized early or in more acute infections developing before the wound lips are healed firmly, spreading the original wound wide apart and keeping it open allows healing by secondary intention in a short time.

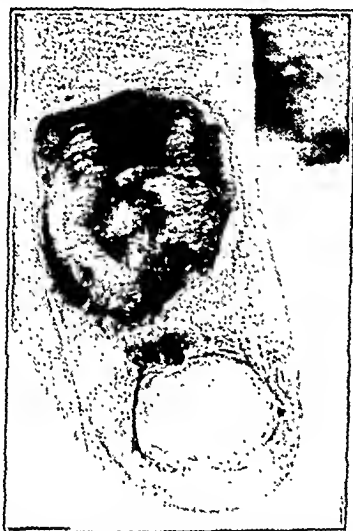


Fig. 1.—Acute dorsal digital subcutaneous bursitis over distal joint of fifth finger. The bursa was unroofed with a sharp scalpel five days before photograph. The exposed bursa appears as the central depressed area, its walls no longer sharp and steep and with healing under way.

The series of bursae here reported measures 3 by 3 mm. in average diameters. After unroofing them, they are easily recognized as a punched out crater, 3 or 4 mm. deep. The lining membrane is glistening gray without visible slough or fibrin. The wound secretion is viscid, clear, or purulent. These bursae were found most frequently in young adults (average age, 30.1 years) and more often in men (24 cases) than in women (3 cases). While butchers, fishermen, and warehousemen form the majority of these patients, housewives or stenographers may develop digital bursitis.

The metacarpophalangeal bursae are the most frequent sites of bursitis of the fingers. Thirteen metacarpophalangeal bursitis cases were observed, 3 of which had simultaneous infection of the adjoining

A proctoscopic examination was made in 58 cases. In 36 of these cases the polyps which were removed surgically were seen on proctoscopic examination. In each case the proctologist stated that the polyp could not be removed safely through the proctoscope. In 21 cases the proctologist fulgurated polyps in the rectosigmoid or rectum.

A satisfactory roentgenoscopic examination was conducted in 56 cases. The polyps were discovered in 50 cases. The 6 patients among whom the roentgenologist failed to obtain evidence of polyps were examined before a satisfactory roentgenographic technique for demonstrating polyps of the colon was developed.

#### SURGICAL TREATMENT

Three days prior to operation the patient was hospitalized. Preoperative preparation consisted in the administration of a nonresidue, high carbohydrate diet, colonic irrigations twice daily, sodium phosphate orally and vaccine intraperitoneally. At operation the diseased portion of the colon, as indicated by the roentgenoscopic and proctoscopic examinations, was exposed and the polyp was located by palpation. In cases in which the polyp was very small, or in cases in which the patient was obese and epiploic tags felt like polyps, the lesion was located by transillumination of the colon with the Cameron light. When the polyp was identified definitely, the diseased portion of the colon was isolated between the rubber-covered blades of a curved clamp. This portion of the colon was packed off carefully from the remainder of the peritoneal cavity. Usually the colon was incised in a longitudinal band for a distance of about 2 cm. The polyp was delivered from the colon. The stalk of the polyp was crushed by a forceps, the base was ligated, and the polyp was excised by using either a knife or cautery. The wound in the colon was closed with two rows of chromic catgut sutures. Epiploic tags, when available, were tied over the line of suture. In an occasional case in which the possibility of soiling the peritoneal cavity existed, a soft rubber tube was employed as a drain. Postoperatively fluids were administered parenterally until the patient passed gas by rectum, at which time the patient was permitted to drink fluids. A rectal tube was inserted frequently to facilitate the passage of gas. The patient was gradually permitted to eat a nonresidue diet which was cautiously replaced by a normal diet.

#### PATHOLOGY

A single polyp was removed in 57 cases. Two polyps were removed in each of 4 cases and in 1 case four polyps were removed. The polyps were situated in the sigmoid in 42 cases, in the descending colon in 15 cases, in the transverse colon in 3 cases, and in the cecum in 3 cases.

## TRANSCOLONIC REMOVAL OF POLYPS

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*(From the Division of Surgery, the Mayo Clinic, and the Mayo Foundation)*

THE present study is concerned with those cases of polyposis of the colon in which the polyps were removed surgically through a small incision in the colon. Only those cases were selected in which the polyps were limited to a small segment of the colon and in which they were situated too high in the bowel to be removed through a proctoscope or sigmoidoscope. The clinical aspects, laboratory data, surgical treatment, pathologic observations, and results of treatment as judged by follow-up studies five or more years after operation are considered.

### CLINICAL ASPECTS

Of the 62 patients studied, 31 were males and 31, females. The average age of the patients was 50.7 years. The oldest patient was 71 years of age and the youngest, 10 years of age.

The outstanding presenting symptom in these cases was bleeding from the rectum; 57 of the 62 patients complained of this symptom. The bleeding was usually intermittent and at times amounted to as much as 1 or 2 ounces of bright or dark blood. The patients often stated that bleeding occurred after a bowel movement. The average duration of the bleeding was thirty-three months. In one case bleeding from the rectum had occurred for ten years.

Symptoms other than bleeding from the rectum were not characteristic of these cases. Eleven patients complained of diarrhea. Constipation occurred in 12 cases. Four patients complained of alternating diarrhea and constipation. Twenty-eight patients suffered abdominal distress which varied widely in situation, character, and severity. In 2 cases bouts of severe abdominal cramps were associated with intussusception. One patient who at operation was found to have a polyp of an intussuscepting type did not experience abdominal distress.

### LABORATORY DATA

Despite the long duration of the bleeding from the rectum, the average concentration of hemoglobin in these cases was 14 gm. per 100 c.c. of blood. The value for hemoglobin in the case in which the most severe degree of anemia was found was 8 gm. per 100 c.c. of blood.

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## COMMENT

The cases presented are a highly selected group. Most of the solitary polyps of the colon are low enough in the bowel to be removed through the proctoscope. During the past decade the proctoscopist has increased his field of operation by employing careful technique and the cases in which polyps of the colon must be removed abdominally have been proportionately fewer than in previous decades.

The patients studied were usually of middle age; representation of the sexes was about equal. Bleeding from the rectum was the only characteristic symptom presented by these patients. The long duration of the bleeding was striking; one patient had been bleeding from the rectum for ten years. It is equally striking that despite the long duration of their bleeding these patients had only slightly reduced values for hemoglobin. Cessation of bleeding from the rectum offered an index of cure after operation; in 8 of 11 cases further bleeding from the rectum did not occur after the polyps had been removed.

Roentgenoscopy and proctoscopic examinations were two of the most important means of diagnosing polyps of the colon. As Buie has stated, during the past ten years the accuracy of both of these examinations has increased greatly. The proctologist's advantage lay in the fact that he was able to view the polyps directly. Since, in the cases studied, polyps were situated too high in the colon to be removed safely through the proctoscope, it is remarkable that the proctologist was able to see 62 per cent of the polyps which were removed.

The roentgenoscopic examination was a particularly valuable diagnostic measure in the present series of cases because the polyps were situated near or beyond the reach of the proctoscope. The 6 patients, among whom the roentgenologist did not discover the polyps, were all examined prior to the use of the air insufflation technique of Weber. Buie cited a case to illustrate the accuracy of the roentgenoscopic examination. A patient whose proctoscopic examination was negative was found by the roentgenologist to have several small polyps in the colon. On re-examination the proctologist found and fulgurated the polyps. The roentgenologist then was not able to find more polyps in the colon.

The roentgenoscopic and proctoscopic examinations were the most important means of determining whether the disease had been eradicated. That such a decision may be very difficult to make was shown by the case in which rectal bleeding continued after the operation and neither the roentgenologist nor the proctologist was able to demonstrate disease in the intestinal tract.

The fact that in 39 of the 62 cases malignant polyps were removed indicates the danger involved in keeping under observation a patient who has polyps of the colon. Although the malignant lesion was of a

One patient had polyps in the transverse colon as well as in the sigmoid. In 39 cases the polyps were malignant. Thirty-one of the malignant polyps were graded according to the method of Broders. Twenty-seven were Grade 1 and 4 were Grade 2 (on a basis of 1 to 4).

#### RESULTS OF TREATMENT

There were 2 postoperative deaths or a surgical mortality rate of 3.2 per cent. The cause of death in one case was peritonitis and in the other case pulmonary embolus and bronchopneumonia.

The postoperative course of 19 patients was noted for periods varying between five and eighteen years. The living patients numbered 14, of whom 5 had malignant lesions and 9 had benign lesions. Among 11 of the living patients a more detailed follow-up study was possible. Eight of these patients were well, had not required further operation, and had not noted bleeding from the rectum since operation. In 3 cases further bleeding from the rectum had occurred. One of these patients was re-examined at the clinic. Roentgenoscopic and proctoscopic examinations failed to reveal the source of the bleeding. This patient was advised to return frequently for examination. Another patient who had had further bleeding from the rectum had a peptic ulcer after a posterior gastroenterostomy had been performed and the possibility of the presence of a bleeding jejunal ulcer was not excluded.

Five patients were dead. Only 1 of the patients who were not living had originally a benign lesion. One patient whose original polyp was malignant and was situated in the sigmoid returned to the clinic three years after his operation and on surgical exploration he was found to have carcinoma of the rectosigmoid with extensive metastasis to the liver. This patient died a few months later. Another patient whose lesion was malignant returned to the clinic one year after her operation and when the surgeon opened her abdomen he found a carcinoma at the junction of the cecum and ascending colon. He stated that undoubtedly the lesion had developed from a polyp. Metastasis had occurred to the liver. The original polyps were removed from the transverse colon and sigmoid. Either the polyp in the ascending colon was not present or was not discovered at the time of the first operation. The patient died three years after her primary operation.

One patient whose polyp was malignant died of myocarditis. Another patient from whom a malignant polyp had been removed was reported dead of an unknown cause.

The only patient not living whose lesion was benign died after surgical exploration of the abdomen in a distant city. A tumor of unknown origin was found in the liver.

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## A NEW CLAMP FOR THE DEVINE COLOSTOMY

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UNDOUBTEDLY, one of the most important advances that has been made in surgery of the large bowel is the preliminary performance of a new type of colostomy devised and advocated recently by Sir Hugh Devine.<sup>1</sup> Indeed so significant is this procedure that it may even be considered revolutionary. Its obvious rationale and perfectly logical conception are immediately apparent. Based on the principle that a completely isolated segment of bowel which is thus deprived of its function loses most of its bacterial content in a relatively short period of time, the colostomy is performed with the purpose of preparing an involved segment of the colon for its subsequent safe extirpation. The procedure, by "defunctioning the distal colon," actually converts a highly dangerous operative area teeming with pathogenic microorganisms into a relatively sterile and safe one. We are so impressed with its surgical rationale and fundamental advantages that it has become a routine preliminary procedure on the Tulane Surgical Service in these cases.

A more detailed account of the principles, technique, and indication of the procedure will not be discussed here, as this is presented in another publication in which is also given our experience in twenty-six cases<sup>2</sup> and a modification of the operation.

In brief the colostomy is performed by making a long spur (8 to 12 cm.) in a loop of the colon proximal to the involved area, dividing the bowel, and inserting the two ends in separate openings in the abdominal wall. Thus the proximal and distal colostomy openings are completely separated or "disconnected" by approximately 4 cm. of skin surface. The fecal stream is completely diverted and spillage into the distal segment is absolutely obviated. Moreover, by frequent lavage of this isolated segment through the distal colostomy opening, the "debacterilization" process can be materially enhanced. Thus the resection can be performed in a practically sterile field.

After the surgical procedure in the involved segment has been completed and healing has occurred, continuity of the bowel is re-established. Devine accomplishes this by a specially devised enterotome with elbowlike curves between the crushing blades and the handle. The blades are separately introduced in the respective colostomy openings, connected by a pivot screw, and, as the handles are gradually drawn together by a wing nut, the crushing blades approximate each

<sup>1</sup>Received for publication, December 6, 1938.

low grade, that it was dangerous was shown by the fact that two patients returned to the clinic and were found to have a malignant lesion and metastasis.

Compared with other surgical procedures, transcolonic removal of polyps is a relatively rare operation for malignancy of the colon. A sufficient number of cases have not been studied to determine whether or not this procedure is sufficiently extensive for use in dealing with malignant polyps of the colon. It was encouraging that 14 of the 19 patients whose postoperative course was followed for five years or more were living. Nine of the 14 patients, however, had benign polyps removed. In only 2 of the 5 cases which terminated fatally could one be sure that the cause of death was malignancy of the colon. In the case of the patient who returned to the clinic three years after his operation and was found to have extensive malignant lesions at the site of the original polyp, a more extensive surgical procedure might have yielded a better result.

#### CONCLUSIONS

A very small number of solitary polyps of the lower portion of the colon cannot be removed by the proctoscopist and must be removed by a transcolonic procedure. The risk of the operation, which in the present series of 62 cases was 3.2 per cent, is justified because in 39 of the 62 cases the polyps were malignant. Of the 19 patients whose course was followed for five to eighteen years after operation, 14 were living. Of the 5 not living, it is certain that 2 died of malignant lesions of the colon.

Bleeding from the rectum, which was the most characteristic symptom presented by the patient, is also valuable as an indication of cure after operation. Roentgenoscopic and proctoscopic examinations, the most valuable aids in the diagnosis of polyps of the colon, are necessary to determine whether or not the disease has been eradicated.

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tively shorter lengths. This facilitates assembly. The upper crossbar is fitted first into its corresponding opening in the other arm of the clamp which it then slides along until the lower crossbar meets its corresponding opening. This arm of the clamp then slides along both crossbars of the other arm of the clamp until the middle screw bar meets its corresponding opening and by turning the wheel the two arms of the clamp are drawn toward each other. Also as the screw wheel is turned, the crushing blades approximate each other until they gradually cut through the spur (Fig. 2). The lower crossbar is so calibrated that it is possible to determine at a glance the exact distance between the two crushing blades beneath the skin surface (Figs. 1, *D*, and 2).

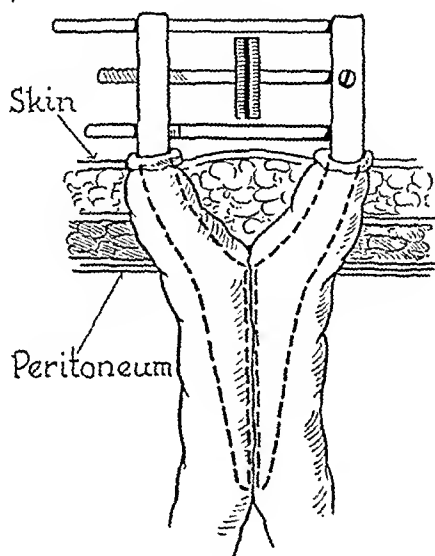


Fig. 2.—Diagrammatic illustration of assembled clamp in the colostomy.

The instrument is constructed of duraluminum to give lightness in weight. As the clamp consists of only two working parts, assembly and disassembly are considerably facilitated. The two crossbars assure stability, smoothness of operation, and an evenly distributed crushing surface. The crushing force is gradually and easily applied by the wheel screw. It can also be readily determined and constantly controlled by the calibrations on the lower crossbar. Because of its lightness in weight and the fact that the handles project only about 3 or 4 cm. above the skin surface, it is extremely convenient, simply requiring an ordinary dressing. Thus it causes no inconveniences or discomfort and the patient can be walking about while it is applied.

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other. In a few days the blades have cut through the long spur between the proximal and distal limbs of the bowel and continuity is re-established.

This type of clamp has been used in our cases and has been found to have certain disadvantages. It is somewhat bulky and inconvenient. Because of its weight and the long handles which project above the skin surface, it tends to fall on its side unless supported by a specially constructed bandage. For the same reason it causes discomfort and pain, probably because of traction on the mesentery.

Ideally the clamp should be so constructed as to possess lightness in weight, simplicity in design, facility in application, and convenience in operation. Moreover, it should create a graduated, evenly distributed pressure along its crushing surfaces on the spur. With this objective in mind, we have devised a clamp which is believed to fulfill these desiderata.

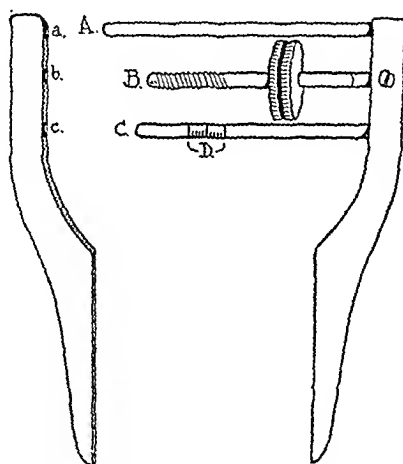


Fig. 1.—Drawing of the two parts of clamp disassembled.

The clamp is constructed of duraluminum and consists of two somewhat S-shaped arms (Fig. 1). The upper parts of these arms serve as handles for the clamp and the crushing surface which is longitudinally grooved is on the lower part. Two right angled crossbars (Fig. 1 A and C) are rigidly attached to the handle of one arm of the clamp. Corresponding openings (Fig. 1 a and c) are present in the other arm of the clamp through which these crossbars slide. Between these two crossbars is a screw provided with a wheel (Fig. 1 B) and also firmly attached to the arm of the clamp but so arranged that it turns freely. A corresponding screw opening is present in the other arm of the clamp (Fig. 1 b).

The technique of application is extremely simple. The two blades of the clamp are greased and separately introduced into the respective colostomy openings. It will be observed from the illustration that the upper crossbar, the lower crossbar, and the screw bar are of respec-

the lesion is caused by some organism yet to be discovered seems improbable. Pathologists variously describe submucous inflammation, an infiltration with small round cells with certain changes in the connective tissue. These descriptions are not always identifying and diagnostic, yet they differ from those of other types of cystitis and vesical ulcer.

Here then is an entity with unique symptoms and a definite cystoscopic picture. Therapeutic experience only has been added to our clinical knowledge of the condition since Hunner clearly described it. We know that recurrence usually follows surgical resection, that overdistention is beneficial, and that, when combined with fulguration persistently and regularly, it is curative. We do not know what causes the lesion nor why it responds favorably to this form of treatment. Its origin, production, and development remain as obscure and baffling as when first called elusive by Hunner, although he meant only cystoscopic elusiveness.

Why does Hunner ulcer affect mostly women and why mostly those between the ages of 30 and 40 years? Why are all males and the younger and older females relatively unsusceptible? Why is it so deep rooted and enduring, so chronic and malignant in nature? Why is it so characteristically linear and always so uniformly located? The trigone and vesical neck are never involved. Why not? Is anatomic structure at the bottom of the distribution of lesions and, if so, in what relation? Is it some perivesical factor, such as peritoneal reflection, or some intramural agency related to the line of wear of movable on fixed parts with filling and emptying? (We have often noted that the early lesions of submucous fibrosis seem to follow the line of flexure on itself which the bladder wall makes when it empties and fills.) If position signifies anything, is this anatomic basis of etiology then peritoneal, muscular, arterial, venous, lymphatic, or nervous? Is the lesion infectious, trophic, allergic or what? What possibly can cause it? Nobody knows.

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# Editorial

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## What Causes Hunner Ulcer?

OF ALL the urologic conditions of unknown cause, such as urogenital cancer, prostatic hyperplasia, polycystic kidneys, urinary lithiasis, and so on, the etiology of Hunner ulcer (submucous fibrosis) is the most evasive and annoying. Cancer of the urogenital tract is but part of a big general problem; ignorance of its cause is fully shared and the solution universally sought. The cause of benign enlargements of various portions of the prostate gland in more than one-third of all men over 50 years of age may be definitely related to certain hormonal changes occurring only in this proportion of our male population, or may be analogous to uterine fibroids with a similar basis of origin, but neither cause is particularly mystifying. Polycystic kidneys arise obviously from some developmental mishap, and the mental exercise of choosing, among the many theories offered in explanation, that one most applicable somehow appeases the urge for knowing the truth. Even more intelligible are the metabolic theories of stone formation and, while all the facts of causation and all the steps of formation of both polycystic disease and urinary lithiasis await discovery, enough is known to blunt one's curiosity. About other conditions of unknown cause, even those for which one guess is as good as another, someone generally comes close enough to satisfy ordinary inquisitiveness. The pathogenesis of Hunner ulcer, however, continues to be a mystery.

Too frequently Hunner ulcer is overlooked by the cystoscopist, the condition being completely unrecognized. Just as often, because of some supposed resemblance, he mistakes its identity and confuses it with some other condition. The diagnosis is purely clinical and can easily be missed or muddled. Only when uncomplicated are the symptoms pathognomonic and as a rule the visual picture is typical only before treatment. Then, frequency with pain, day and night, a clear urine, nothing more, point to a Hunner ulcer and, on looking in, a narrow line of inflammation is found on the dome of the bladder or at the side above one or the other ureteral orifice or, when extensive, arching clear across from above one orifice to above the other; a line of inflammation characterized by a seemingly intact mucosa which bleeds on the least vesical distention. The urine may show a few red blood cells but usually, before cystoscopy, is clear both macroscopically and microscopically, and no growth is found on culture. Even cultures of tissue from the inflamed area (taken by cystoscopic rongeur and at operation) generally show neither aerobes nor anaerobes. That

out beyond the anus. Today anorectal operations can be approached both by the patient and by the surgeon with no greater apprehension of suffering than that which may accompany any other surgical procedure.

At the present time it would appear that the application of ambulant treatment to anorectal disorders is overstressed. To be sure, great advances have been made in the office management of minor surgical procedures, chiefly by the utilization of newer methods of prolonged anesthesia. This is in many instances justifiable and praiseworthy. But the result is all too often inadequate surgery with resultant delay in proper alleviation of the condition.

The medical literature of today contains annually hundreds of articles on diseases of the anorectal region. To undertake a review of the advances in all phases of the subject is beyond the scope of this paper. Attention has therefore been directed to a discussion of certain common disorders. Conflicting opinions naturally exist in a field which is served by the general surgeon and by the proctologist who may not have had the benefit of general surgical training. Personal opinion undoubtedly influences such a review, but this is unavoidable.

#### ANESTHESIA

Complete muscular relaxation is essential for efficient anorectal surgery. Relaxation of the sphincter and levator ani muscles allows the anal canal to open up and evert, resulting in proper exposure with an absolute minimum of pulling and retraction of tissues—a cardinal principle in this field of surgery. The anal sphincters are the last muscles of the body to relax under any form of inhalation anesthesia and will adequately relax only under deep ether saturation. In addition to the primary hazards of such an anesthetic there are further disadvantages. The frequent resulting nausea and vomiting produce violent distortion of the anal canal which may tear out sutures, displace dressings, and induce hemorrhage. Ether anesthesia also tends to be followed by spasmodic contractions of the anal sphincters<sup>7</sup> with an increase of postoperative discomfort. There is also variable delay in the early resumption of ingestion of fluids and solid foods. Happily, the use of general inhalation anesthesia for anorectal operations has been largely discarded. Nitrous oxide or cyclopropane anesthesia is adequate and desirable for incision and drainage of perianal or perirectal abscesses where no attempt is to be made to investigate or to operate within the anal canal. It may be used also for the occasional highly neurotic individual for analgesia, utilizing some other type of anesthetic for complete muscular relaxation.

The use of *intravenous anesthetics* has achieved a certain popularity, principally for procedures that can be completed within five or ten minutes. Evipal, introduced in 1932,<sup>186</sup> and pentothal sodium, intro-



# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## RECENT ADVANCES IN THE MORE COMMON PROBLEMS OF MINOR ANORECTAL SURGERY

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THE treatment of anorectal disease too long remained in the hands of the charlatan, who glibly promised cures without surgery and dispensed "painless pile dissolvents." To be sure, for many years there have been occasional physicians and surgeons who have labored earnestly in this field, but it is only in the past few decades that any considerable number have concentrated upon the advancement of the understanding of its peculiar problems. Today this advance has attained considerable momentum, and anorectal surgery has achieved a conspicuous place as a specialization in surgery. The modern proctologist is fundamentally a surgeon well trained in the general principles of surgical diagnosis and technique. The vast majority of pathologic conditions occurring in this region must be approached and treated by the special application of general surgical principles.

No advance in such a special field of surgery is possible without increased understanding of the pathologic changes which can and do take place in the region involved. Great progress has been made possible in this respect by increasing general recognition of the importance of complete and careful examination of every patient who presents himself to the physician with any anorectal complaint. It is unfortunately still true that from 26 to 50 per cent of patients with carcinoma of the rectum, within easy reach of the examining finger, still receive treatment for some other supposed rectal condition for weeks and months before the correct diagnosis is made. But the importance of proper examination is now so stressed in medical education that such a record in the future will be inexcusable.

There has been in recent years a tremendous advance in the diminution of suffering which all too often accompanied any anorectal operation. Many new anesthetic agents have been developed to minimize the patient's postoperative discomfort. But of equal importance has been the intelligent application of certain principles in the technique of the operation itself: avoidance of undue trauma, avoidance of entaneous sutures, and adequate surgical drainage of all wounds well

anus in the midline in three planes, one backward in the midline deep and paralleling the anal canal for a distance of  $1\frac{1}{2}$  inches, and one on either side deeply forward and outward  $2\frac{1}{2}$  to 3 inches. Similarly, through a point 1 inch anterior to the anus in the midline, the needle is passed upward  $1\frac{1}{2}$  inches parallel to the anal canal in the midline and then on either side deeply backward and outward  $2\frac{1}{2}$  inches, injecting a total of 15 to 20 c.c. of the anesthetic solution. A gloved finger is kept in the rectum during all of this procedure to be certain that the needle at no time pierces the anal skin or the mucous membrane above. The posterior injection serves to block the posterior branches of the inferior hemorrhoidal nerves, the anococcygeal nerves, and the perineal branch of the fourth sacral nerves. The anterior injection serves to block the posterior serotal nerve, the lateral terminal branches of the perineal nerve, and the anterior branches of the inferior hemorrhoidal nerves. Complete relaxation and anesthesia ensue.

*Caudal anesthesia* has not been widely used in anorectal surgery because of its variable effectiveness, with failure of satisfactory anesthesia and relaxation in from 4 to 25 per cent of cases reported.<sup>13, 14, 78, 146, 160</sup> The theoretical advantages are those of a nicely controlled level of anesthesia, which is extradural, with none of the undesirable reactions occasionally associated with spinal or intradural anesthesia. Renewed interest recently has been shown in this method by Reuther,<sup>147</sup> who had no failures using 2 per cent metycaïne, although he had had 55 per cent of failures using freshly prepared alkaline procaine.

*Sacral block anesthesia*, by combined caudal and transsacral block, has been proved to be a safe and effective method in the hands of those experienced in its use. This method has long been advocated by Buie,<sup>30</sup> who after 15,000 cases considers it the ideal anesthesia. Failure of its universal acceptance as the ideal anesthetic is essentially due to the fact that the method is time consuming, requires patience and the skill born of experience on the part of the anesthetist, and is more trying to the patient than the single introduction of a lumbar puncture needle. The method is used today by relatively few surgeons, although its adequacy and safety have for many years been demonstrated in the department of proctology at the Mayo Clinic. Block anesthesia of the sacral nerves as described by Buie<sup>28</sup> consists in the injection of 25 c.c. of 1 per cent procaine with 1 per cent of a 1:2,600 solution of epinephrine into the caudal canal, followed by injection of 15, 10, and 3 c.c. of the same solution respectively into the second, third, and fourth sacral foramina on either side. Anesthesia is to be expected in ten or fifteen minutes, will be intense in twenty to thirty minutes, and will last one to two hours.

*Spinal anesthesia* is considered by many to be the anesthetic of choice, producing prompt anesthesia and extreme relaxation with minimal discomfort to the patient in the course of induction. Improved

duced in 1935,<sup>112</sup> are the agents of choice. Their action is characterized by ease of administration, rapidity of induction of deep anesthesia, complete muscular relaxation, short duration of anesthesia, prompt recovery, adequate margin of safety, and rare after-effects.<sup>47, 81, 82, 111, 112</sup> Smoother action, less noticeable fall in blood pressure, quicker recovery, less subsequent amnesia are claimed for pentothal sodium by Haskell,<sup>81</sup> who has found anesthesia satisfactory in 85 per cent of 175 anorectal operations requiring less than ten minutes of anesthesia. Attention has been called<sup>47, 82</sup> to the variable period of amnesia following anesthesia lasting thirty minutes to twelve hours. This must be seriously considered in the application of this method of anesthesia to office procedures. Technique of administration is adequately detailed by Lundy,<sup>111</sup> Bacon,<sup>7</sup> and Haskell.<sup>81</sup> Contraindications for its use are hepatic disease, low blood pressure, any condition which produces gross interference with gaseous interchange in the lungs, idiosyncrasy to barbiturates, and extreme youth or old age.<sup>7, 47, 82</sup> Haskell and Cheleden<sup>82</sup> have collected 32 fatalities from the literature in several hundred thousand administrations.

The usefulness of this form of anesthesia would appear to be definitely limited to procedures requiring but a few minutes and necessitating good sphincter relaxation, such as the control of hemorrhage, incision of abscess, or removal of fecal impaction.

*Regional Anesthesia.*—Anesthesia with complete muscular relaxation is best achieved by interruption of the sensory and motor pathways at one point or another along the course of the nerves from the spinal cord to the terminal nerve fibrils.

*Local infiltration,* "free injection and saturation of tissues immediately adjacent to and beneath the field of operation or just proximal to the sensory nerve endings,"<sup>7</sup> is undesirable<sup>28</sup> except for the excision of a thrombosed external hemorrhoid, the removal of a papilla, or the trimming of cutaneous tags. There are two major objections: resultant deformity of the tissues and the danger of subsequent infection from contiguous inflammation.

*Conduction anesthesia,* or blocking of the conducting pathways proximal to the terminal nerve distribution, is a popular method of anesthesia. Although this is frequently referred to as local anesthesia, it differs from local infiltration in that the anesthetic solution is injected deep to the sphincter muscles without deformity of the more superficial tissues and with a minimal danger of subsequent infection. It is applicable in most minor anorectal operations with the notable exception of fistulotomy. Here the hidden possibility of extension of infection into the region of infiltration is a definite hazard and contraindication to its use. The technique of conduction anesthesia is described in detail by Bacon.<sup>7</sup> Introduction of 15 to 20 c.c. of anesthetic solution is made posteriorly through a point  $1\frac{1}{2}$  inches back of the

*Lumbar epidural or peridural anesthesia* has received no particular attention as yet for anorectal surgery but in the future may prove to be highly satisfactory. Although the idea of epidural anesthesia was conceived in 1885 by Corning<sup>41</sup> and used in 1920 by Pagés,<sup>142</sup> a satisfactory method of localizing the peridural space was not discovered until 1928<sup>85</sup> and its usefulness not recognized until 1932, when Gutiérrez<sup>72</sup> enthusiastically reported its use in over 3,000 patients. Further favorable reports have been made by Dogliotti,<sup>45</sup> Harger,<sup>77</sup> and Odom.<sup>141</sup> This type of anesthetic is comparable to caudal and transsacral block anesthesia accomplished by a single needle puncture in the lumbar region, but without the possible complications of intradural spinal anesthesia. The hazard of this method lies in inadvertent puncture of the dura and possible injection of 20 or more c.c. of novocaine solution into the spinal canal.

*Anesthetic Agents.*—A tremendous enthusiasm is evinced in the literature of the past several years for the use of anesthetic agents which have the property of prolonged action for the reduction of postoperative discomfort. Before discussing the numerous agents that have been used for this purpose, it is worth pausing to consider critically the utilization of such measures. Great strides have been made in the reduction of postoperative pain by improvements in preoperative and postoperative care, the now almost universal elimination of the large rectal retention tube or "whistle tube," and above all by appropriate surgical technique performed under adequate anesthesia and relaxation. In not a few hands these measures alone have been entirely satisfactory in effecting a uniformly comfortable postoperative course. Too free use of anesthetizing agents of prolonged action must not be stressed to the exclusion of superior surgical technique. That this occurs is obvious in scores of published reports in which the importance of the particular anesthetic agent used overshadows the importance of the surgical procedure employed. Most of the solutions advocated are definitely tissue irritants; many of them have produced, at least occasionally, actual necrosis. Such measures violate one of the cardinal principles of anorectal surgery; namely, the avoidance of all undue trauma, physical, thermal, and chemical.<sup>125</sup> The danger of complicating infection as the result of the injection of a slowly absorbed solution contiguous to wounds which are often primarily and always secondarily infected must always be considered. There is, on the other hand, no excuse for universal condemnation of measures which may be of real assistance in the reduction of postoperative sphincter spasm and discomfort. Provided the hazards and pitfalls of such measures are always kept in mind, there is unquestionably a use for such agents. Great progress has already been made and further progress is to be expected in this field.

technique and the refinement of drugs employed has resulted in greater safety than in general anesthesia.<sup>22, 53, 59</sup> The alarming fall in blood pressure so frequently encountered in the use of high spinal anesthesia does not occur if it is restricted to the lower lumbar and sacral levels.<sup>4</sup> Diffusion of the anesthetic agent to high levels is dependent principally on the effect of gravity. Control of the level of anesthesia can therefore be satisfactorily accomplished by proper adjustment in the position of the patient, the head and shoulders being kept below the level of the hips when an anesthetic agent lighter than spinal fluid is employed or slightly above this level when the anesthetic agent is heavier than spinal fluid. An increased frequency of urinary retention is said to follow the use of spinal anesthesia.<sup>7</sup> This complication, however, is more closely correlated to the intensity of postoperative pain and the degree of sphincter spasm than to the type of anesthesia employed. The one real and annoying complication is "postspinal" or "meningeal" headache, which has been variously estimated<sup>40, 99, 136, 178</sup> as occurring in from 4 to 32 per cent of cases. Such headaches are not noted in patients who remain in bed for a week or more. But the average patient, following a minor anorectal operation, is allowed out of bed on the second, third, or fourth day and may promptly develop headache after he has been up. It is controllable by prompt return to the horizontal position and usually does not recur after two or three days. The occasional persistence of this symptom for one or two weeks can be the source of considerable annoyance to the patient and embarrassment to the surgeon. Although disputable, such headaches would appear to be associated with the leakage of cerebrospinal fluid through the needle puncture in the dura. It is notable that the patient who tosses himself about in bed and insists upon raising his head and shoulders and even sitting up in bed is much more apt to develop headache than the patient who lies quietly flat in bed for twenty-four to thirty-six hours. Some time ago I became discouraged with the use of spinal anesthesia because of the frequency of postspinal headache, although I considered this type of anesthesia as otherwise ideal. However, since the employment of a 23 gauge lumbar puncture needle and insistence upon strict horizontal position of the patient for thirty-six hours following operation, this annoying complication has practically vanished. Relief of postspinal headache is said to be achieved by pilocarpin sweats,<sup>54</sup> pituitrin or caffeine citrate,<sup>7</sup> intravenous caffeine sodium benzoate,<sup>122</sup> or 0.5 per cent solution of nitroglycerin in alcohol.<sup>16</sup> Nausea and vomiting have been noted in 5 per cent<sup>50</sup> to 15 per cent<sup>98</sup> of cases having spinal anesthesia. This is more prone to occur in nervous and apprehensive individuals and occurs practically always in women. The administration of morphine preoperatively appears often to be a factor in this condition and other medication is recommended, preferably one of the barbiturates.

*Nupercaine hydrochlorid*, or *percaine*, a quinoline derivative, is considered by some<sup>107, 183</sup> to be more toxic than cocaine and ten times more potent. Bacon,<sup>5</sup> after using it in 91 cases for conduction anesthesia, reports results superior to novocaine: injection painless, prompt anesthesia lasting 6 to 6½ hours, no local irritation, and no untoward effects; 1:1,500 dilution is recommended. Keyes and McLellan<sup>103</sup> report analgesia lasting 6 to 8 hours. Jones<sup>100</sup> recommends percaine 1:1,500 for spinal analgesia.

*Diothane*, a derivative of phenyl urethane, was suggested by Rider<sup>151</sup> for prolonged anesthesia in 1930. This authority concludes<sup>150</sup> that when used subcutaneously it approximates procaine in toxicity, is relatively stable to heat and can be sterilized by boiling, has considerable bacteriostatic action, but must be prepared and kept in nonalkaline containers (pyrex glass) to avoid precipitation of free base. After careful study in 100 cases, Rosser<sup>154</sup> is of the opinion that 0.5 of 1 per cent diothane in an isotonic solution produces relatively little irritation and gives anesthesia lasting from several hours to several days. Because of the immediate discomfort upon injection, he suggests combination with procaine for infiltration anesthesia for such minor procedures as the excision of a thrombosed external hemorrhoid. He has found it to be very efficacious in the reduction of postoperative sphincter spasm and discomfort by conduction block immediately following hemorrhoidectomy under spinal anesthesia. It should never be used as a spinal anesthetic agent because of an apparent chemical incompatibility with spinal fluid. Smith reports<sup>169</sup> that a 1 or 0.5 of 1 per cent solution diffuses slowly in the tissues and must be distributed carefully to prevent pooling and possible slough. Anesthesia is slow (10 to 15 minutes). He finds definite decrease in postoperative discomfort by conduction block with 5 to 10 c.c. of 0.5 of 1 per cent solution immediately following operation under some other form of primary anesthesia. Bacon,<sup>7</sup> using 5 c.c. of 0.5 of 1 per cent solution of diothane for posterior conduction block immediately following operation under spinal anesthesia, reports an average duration of anesthesia of 90 hours in 118 patients. These patients had varying degrees of discomfort but no severe pain. Other favorable reports on the use of diothane have been made by Terrell,<sup>180</sup> Simmons,<sup>164</sup> and Hertzler.<sup>88</sup>

*Tutocaine hydrochloride* is considered to be twice as potent as procaine hydrochloride and one-half as toxic. Kilbourne<sup>104</sup> recommends its use as a 2.5 per cent solution for prolonged anesthesia.

*Anesthetic Agents in Oil.*—Numerous anesthetic agents are now in use in combination with sweet almond oil for prolonged anesthetic effects. This action depends primarily on the slow rate of absorption of the injected material. In contrast to the water-soluble anesthetic agents of prolonged action with analgesia lasting from several hours to several days, the effect of these preparations in oil is supposed to

The most commonly used anesthetic agent for all types of regional anesthesia is novocaine or its prototype, procaine. For local infiltration and conduction anesthesia a 0.5 to 1 per cent solution is employed. For caudal and transsacral block a 1 to 4 per cent solution is used. For spinal anesthesia 25 to 60 mg. dissolved in 1 to 3 c.c. of fluid is customary. No anesthetic agent has yet been developed that is more effective, prompter in action, or less toxic. The rapidity of cessation of anesthesia is as great as its induction, regardless of the method of administration employed. This often is followed immediately by a period of hypersensitivity and spasmodic contractions of the sphincter ani muscles. Patients in whom the subsequent postoperative course is entirely comfortable may suffer considerable discomfort during a variable period of time shortly after their return from the operating room. It has been thought that the utilization of an anesthetic agent, the effects of which wore off more gradually over a longer period of time, might eliminate this disadvantage.

*Quinine and urea hydrochloride* was popularized for its prolonged anesthetic action early in the twentieth century. It was abandoned by the general surgeon because of the resulting induration, edema, and sometimes sloughing, but it is still used by some in anorectal surgery.<sup>87, 188</sup> Originally used in a 5 per cent solution,<sup>67, 69, 93, 192</sup> it subsequently was advocated in a 0.25 to 1 per cent strength.<sup>157, 158</sup> Saphir, after extolling its use as the "ideal local anesthetic"<sup>157</sup> for hemorrhoidectomy in over 2,000 cases, abandoned it<sup>159</sup> because of the immediate production of fibrin, delay in healing, and sloughing of tissues and returned to 0.5 per cent novocaine with 2½ minims of adrenalin to the ounce. In any effective strength it tends to cause considerable pain on injection, analgesia is slow to appear (5 to 20 minutes), and it is definitely irritating, producing variable degrees of tissue reaction with not infrequent necrosis and slough.<sup>104, 159</sup> The anesthetic action is said to last from two to ten days.<sup>157, 188</sup>

*Quinine hydrochloride and urethane* has been found by Kilbourne<sup>101</sup> to be a less painful and less irritating solution than quinine and urea hydrochloride.

*Eucupin*, a quinoline derivative, in 1:1,000 dilution in combination with 0.5 per cent procaine, was advocated by de Takats<sup>41</sup> in 1926 for its prolonged action and gradual cessation of analgesia. Mannheim and Marks<sup>115</sup> in 1938 reported reliable anesthetic action for minor anorectal surgical procedures with eucupin dihydrochloride 0.1 per cent combined with procaine hydrochloride 1 per cent in saline solution, producing postoperative analgesia of three to seven days. Eucupin, 0.75 per cent in distilled water, has been found by Kilbourne<sup>101</sup> to relieve postoperative pain by topical application in wet dressings applied directly to anorectal wounds immediately following operation.

action, itching and local urticaria) in 3.04 per cent, and reaction due to technique of injection (superficial necrosis and deep abscess) in 1.17 per cent of cases. In the majority of cases he has used 5 to 10 c.c. of the solution for supplementary anesthesia, but in some it has been employed for primary anesthesia.

*Neothsol*, composed of procaine base, 1 per cent; methyl methylene para-amino-phenylformate, 2 per cent; hydroxbenzocarbinal, 5 per cent; in refined French almond oil, is considered superior by Burt and Rennie.<sup>32</sup> He considers 15 to 20 c.c. adequate for most operations and 25 c.c. sufficient for hemorrhoidectomy, subcutaneous circumanal injection giving complete anesthesia of the skin. In a series of 194 cases, 6 per cent developed necrosis of tissue; 2 had generalized reactions.

*Nupercaine base*, 1.5 per cent; benzyl alcohol, 10 per cent; phenol, 1 per cent; in sterile sweet almond oil is recommended by Steinberg.<sup>174</sup>

#### HEMORRHOIDS

It is the deliberate intention of the author to omit from this review all discussion of etiology, predisposing factors, incidence, descriptive anatomy, classification, symptomatology, and diagnosis of hemorrhoids. These subjects are thoroughly discussed in standard textbooks on the subject. The introductory paragraphs of the chapter on hemorrhoids in Buie's *Practical Proctology* are recommended for reading to anyone interested in the subject of treatment of hemorrhoids.

There has been increasing recognition of the fact that true appreciation of the presence and size of hemorrhoids cannot be gained by mere external inspection, nor is digital examination of particular value because of the softness and easy compressibility of internal hemorrhoids. Internal inspection is of prime importance, preferably with an anoscope which has an oblique internal orifice. It has also been increasingly recognized that patients do not actually suffer from hemorrhoids but from the complications of hemorrhoids, and proper treatment must depend upon what those complications are. In the determination of treatment it is important to recognize internal and external hemorrhoids as such. Those situated above the mucocutaneous or pectinate line and covered with mucous membrane are always internal hemorrhoids and those situated below this line and covered by skin are always external hemorrhoids regardless of their relative position inside or outside of the anal canal at the time of examination. All too often the doctor as well as the patient attempts by main force to "redneck" an acutely thrombosed external hemorrhoid, inflicting more harm than good upon the unhappy patient. In the attempt to correlate the symptoms and the physical findings for the determination of proper treatment, it is important to remember that the mucocutaneous line is also the landmark for the upward extent of sensory



last from several days to several weeks. Originally devised for use in treatment of fissure-in-ano and pruritus ani, their use has been extended by some to the control of postoperative pain. These solutions produce variable irritative reactions and must be used with caution. Injection of the solutions at body temperature is recommended to minimize reaction. Some<sup>34, 70, 125, 130, 145</sup> consider that there is no indication for their use in anorectal surgery.

*Benacol*, introduced in 1927 by Yeomans and co-workers,<sup>124</sup> consists of para-amino-benzoyl (ethacaine), 5 per cent; phenmethylo, 5 per cent; rectified sweet almond oil, 90 per cent. The use of this agent in the control of postoperative pain is emphasized by Hayes.<sup>84</sup> Infiltration is attended by burning pain which may last for several hours.

*Gabriel's solution* or A. B. A., introduced as an inexpensive substitute for benacol in 1929,<sup>57</sup> consists of anesthesin, 3 per cent; benzyl alcohol, 5 per cent; ether, 10 per cent in sterilized almond oil. Simmons<sup>164</sup> considers this the best of the oil-soluble anesthetics for the control of pain following hemorrhoidectomy. The use of this solution is not without discomfort to the patient.

*Morgan's solution*, introduced in 1935,<sup>131</sup> consists of procaine base, 1.5 per cent; butyl-para-aminobenzoate, 6 per cent; benzyl alcohol, 5 per cent; in sterile almond oil. Morgan claims painless induction if injected slowly, no severe afterpain, certain and prolonged anesthesia for 7 to 28 days, used in amounts up to 20 to 30 c.c. Reuther<sup>148</sup> has used this solution for anesthesia in minor anal operations, 10 c.c. producing no reaction, with skin anesthesia in five minutes. He found the minimal duration of anesthesia to be 5 days, the maximal duration 23 days, and the average duration 12 days.

*Anucaine*, introduced by Gorsch<sup>66</sup> in 1934, consists of benzocaine, 5 per cent; phenmethylo, 5 per cent; butyl aminobenzoate, 1 per cent; novocaine base, 0.125 per cent; in sweet almond oil. In a later article<sup>63</sup> this authority does not recommend the solution as an operative anesthetic but suggests its use to alleviate postoperative pain. In 3,000 injections, using 5 c.c. in each posterior quadrant and 2 c.c. in each anterior quadrant, he has experienced no slough and no general reactions of any severity, but in several cases there has been transitory induration in the perianal tissues or an urticarial rash in patients presumably sensitive to almond oil. He frequently injects the solution one to two days before operation.<sup>62</sup> Green<sup>70</sup> has made a carefully controlled study of the efficacy of anucaine by estimating the amount of immediate postoperative medication necessary, the frequency of postoperative catheterization, and the spontaneity of the first bowel movement after operation. He concludes that pain is definitely minimized by providing prolonged relaxation of the sphincter muscles. In regard to frequency of complications by its use he reports reactions due to drug sensitivity (prolonged sensory anesthesia, constitutional and local re-

or stenosis as the result of inability to judge the amount of tissue necessary to remove. Cartwright concludes that the danger of embolism and liver abscess is greater without than with operation which is performed under block anesthesia without clamps and without anal divulsion. Lockhart-Mummery<sup>109</sup> favors immediate operation and states that he has never seen any ill effects from such procedures.

*Hemorrhoidectomy.*—Careful perusal of the literature of the past few years does not lead to the impression that the operation of hemorrhoidectomy has yet escaped from its unenviable reputation for postoperative suffering. The various "types" of operation in vogue a hundred years ago all still have their proponents. The exaltation of "ambulant methods" is frequently justified by reference to the prolonged suffering incurred by operation. And yet in actual fact perhaps the greatest advance in "minor" anorectal surgery has been in the operative treatment of hemorrhoids. This has not occurred as the result of a new "type" of operation but by awakening recognition of the fact that hemorrhoidectomy is fundamentally a plastic operation performed upon tissues of peculiar anatomic characteristics in a region incapable of complete physiologic rest and inevitably subject to infection. This principle has been eloquently expressed by N. D. Smith in an article entitled "Hemorrhoidectomy: A Plastic Operation."<sup>171</sup> By the application of this principle Newman<sup>140</sup> finds that only 2 per cent of patients following hemorrhoidectomy require a narcotic and then morphine sulfate gr.  $\frac{1}{6}$  once only. Merar,<sup>125</sup> in 1939, lays down certain rules for hemorrhoidectomy: (1) Avoidance of every form of injury, mechanical, thermal, chemical, (2) application of that expert and particular care to which this area, as one of the most sensitive regions in the human body, is entitled; (3) utilization of a tried and tested routine preoperative and postoperative regime; (4) selection of an open, nonburning, nontraumatizing method of operation. Buie in his book *Practical Proctology*<sup>28</sup> says: "We dispense with formulas and urge that no particular type of operation be applied to all cases . . . rarely is it possible to do any series of operation in the same identical manner. We must adapt ourselves to conditions . . ."

In plastic surgery great emphasis is placed on preoperative preparation and particularly on postoperative care of wounds. This is of vital importance in hemorrhoidectomy and upon this depends in considerable part the postoperative comfort of the patient. Merar<sup>125</sup> emphasizes the importance of preoperative preparation to offset postoperative gas pains and to relieve the patient of any desire to defecate for at least three postoperative days. He recommends 6 ounces of citrate of magnesia twenty-four hours prior to operation, hospitalization the night before operation, with a plain water enema that night followed by a retention enema of 4 ounces of olive oil, to be expelled in the morning and followed by another plain water enema. For a

innervation. When the patient's chief complaint is pain, the cause of this pain must be at or distal to this line and regardless of how big or how vascular or how eroded are his internal hemorrhoids it must be realized that this pain is not going to be relieved by treatment directed solely to the internal hemorrhoids. It is also important to remember that, regardless of how large the hemorrhoids may be, the patient's symptoms may not be from the hemorrhoids at all but may be due to a great variety of other causes, including cancer. Careful and complete digital, anoscopic, and proctoscopic examination should always be performed and a satisfactory cause for all symptoms found, to the exclusion of other possible causes, before any treatment at all is instituted for the hemorrhoids.

In the consideration of the numerous recommended methods of treatment for hemorrhoids, it must be emphasized again that the only satisfactory application of any of these methods will depend upon the surgeon's complete understanding of the true pathologic condition present and the correct application of the proper method of treatment to the particular condition existing.

*Thrombosed Hemorrhoids.*—Thrombosis of external hemorrhoids was long considered to be the result of a mechanical rupture of an anal varicosity with formation of an extraluminal hematoma. Such diffusion of blood in the perianal tissues does occur, but is rare in comparison with the frequency of multiseptated intraluminal thromboses which may result from a tiny tear in the intima of a thin-walled vein but which are probably frequently secondary to infection in the region of the adjacent crypts. Conservative treatment of the small thrombosed external hemorrhoid by rest, hot Sitz baths, and stool lubrication will be followed by gradual resolution and fibrosis in the course of from a few days to a week or more. Decision as to surgical intervention rests upon the judgment of the surgeon and it may well be employed if it is felt that pain and incapacity can be definitely reduced by such a procedure. Incision and expression of the clot are to be discouraged as this rarely shortens the natural course of the disease. Block excision of the multiseptated clots should be done through an elliptical incision in the overlying skin so devised that the edges of the incision will fall accurately together at the end of the operation. If properly accomplished, with no sutures or ties employed, relief is practically complete in less than twenty-four hours.

The advisability of immediate operation in cases of diffuse thrombosis of external and internal hemorrhoids with associated edema, infection, and necrosis is considered questionable. Cartwright<sup>25</sup> discusses the subject thoroughly and analyzes 116 returns on a questionnaire sent to members of the American Proctologic Society. Immediate operation was favored by 76 and 38 considered it inadvisable. Those who practice delay do so because of fear of embolism, liver abscess,

or stenosis as the result of inability to judge the amount of tissue necessary to remove. Cartwright concludes that the danger of embolism and liver abscess is greater without than with operation which is performed under block anesthesia without clamps and without anal division. Lockhart-Mummery<sup>109</sup> favors immediate operation and states that he has never seen any ill effects from such procedures.

*Hemorrhoidectomy.*—Careful perusal of the literature of the past few years does not lead to the impression that the operation of hemorrhoidectomy has yet escaped from its unenviable reputation for postoperative suffering. The various "types" of operation in vogue a hundred years ago all still have their proponents. The exaltation of "ambulant methods" is frequently justified by reference to the prolonged suffering incurred by operation. And yet in actual fact perhaps the greatest advance in "minor" anorectal surgery has been in the operative treatment of hemorrhoids. This has not occurred as the result of a new "type" of operation but by awakening recognition of the fact that hemorrhoidectomy is fundamentally a plastic operation performed upon tissues of peculiar anatomic characteristics in a region incapable of complete physiologic rest and inevitably subject to infection. This principle has been eloquently expressed by N. D. Smith in an article entitled "Hemorrhoidectomy: A Plastic Operation."<sup>171</sup> By the application of this principle Newman<sup>140</sup> finds that only 2 per cent of patients following hemorrhoidectomy require a narcotic and then morphine sulfate gr.  $\frac{1}{6}$  once only. Merar,<sup>125</sup> in 1939, lays down certain rules for hemorrhoidectomy: (1) Avoidance of every form of injury, mechanical, thermal, chemical; (2) application of that expert and particular care to which this area, as one of the most sensitive regions in the human body, is entitled; (3) utilization of a tried and tested routine preoperative and postoperative regime; (4) selection of an open, nonburning, nontraumatizing method of operation. Buie in his book *Practical Proctology*<sup>28</sup> says: "We dispense with formulas and urge that no particular type of operation be applied to all cases . . . rarely is it possible to do any series of operation in the same identical manner. We must adapt ourselves to conditions . . ."

In plastic surgery great emphasis is placed on preoperative preparation and particularly on postoperative care of wounds. This is of vital importance in hemorrhoidectomy and upon this depends in considerable part the postoperative comfort of the patient. Merar<sup>125</sup> emphasizes the importance of preoperative preparation to offset postoperative gas pains and to relieve the patient of any desire to defecate for at least three postoperative days. He recommends 6 ounces of citrate of magnesia twenty-four hours prior to operation, hospitalization the night before operation, with a plain water enema that night followed by a retention enema of 4 ounces of olive oil, to be expelled in the morning and followed by another plain water enema. For a

restful night to reduce preanesthetic fear and psychic trauma, he recommends 3 to 6 gr. of sodium amytal, giving another 3 gr. on awakening and dilaudid  $\frac{1}{20}$  gr. one hour before operation. In regard to postoperative care Smith<sup>171</sup> stresses the importance of gentle cleanliness, the frequent use of nonirritating antiseptics, and the generous application of heat. Frequent hot Sitz baths should be started not later than the third day for cleansing, relaxation of the sphincters, and their soothing and healing effects upon the wounds. There are two noteworthy omissions in present-day postoperative routine: The large retention rectal tube routinely employed a few years ago, and the practice of "tying up the bowels" for several days to a week or more after operation. The "whistle tube" was a constant source of irritation to the wounds and elicited a reflex spasmodic contraction of the sphincters which was harmful to healing and most uncomfortable to the patient. Gentle dilatation of the anal canal is recognized as desirable a few days after operation to prevent adherence of raw surfaces within the canal and to keep the wounds open for proper distal drainage. Dilatation by the insertion of a finger is painful, largely because of the resistance of the sphincter muscles. Such resistance, however, is minimized by the natural coordination of these muscles in the normal physiologic act of defecation. Therefore the early passage of a soft but formed stool will accomplish the desired effect with the minimum of discomfort. To this end it is recommended that the patient be placed upon a regular diet immediately after operation and be given some agar-agar or tragacanth preparation to assure a formed but soft stool. Spontaneous defecation will usually occur on the third or possibly fourth postoperative day and is far more desirable than the use of enemas or more drastic catharsis. Patients may be dismissed from the hospital on the day following the first spontaneous bowel movement. Examination should be done at least twice weekly to be sure that proper healing occurs. On about the eighth day it is desirable gently to introduce the finger into the canal to be certain that spontaneous dilation by bowel movements has been adequate.

The importance of complete muscular relaxation for correct plastic surgery cannot be overstressed. This has already been discussed under anesthesia. The prone ventral position with the hips slightly elevated is recommended<sup>25</sup> to facilitate easy exposure and to provide an unhampered position for the surgeon. The objective of operation is thorough removal of the groups of varicose veins underlying the mucous membrane of the distal portion of the rectum and the skin of the anal canal with satisfactory functional result and a minimal deformity.<sup>171</sup> By careful technique and proper regard for sound principles in the care of infected wounds, all of the hemorrhoids can be removed without producing undesirable distortion or disturbing the function of the parts. Following a properly performed hemorrhoidec-

tomy, hemorrhoids will not recur and it is only when all hemorrhoids are not removed that they do recur.<sup>28</sup> It is important to recognize the fact that sterilization of the operative field is impossible. Therefore all unnecessary tissue damage must be avoided, all tissue which may slough must be removed, and adequate surgical drainage must be provided for.<sup>171</sup> Sutures placed distal to the mucocutaneous line will increase postoperative discomfort, causing induration and edema not conducive to optimal healing, and should not be used. Divulsion of the sphincters is generally disapproved. Merar<sup>125</sup> considers this a major factor in producing severe postoperative pain, stating that the idea of causing temporary paralysis by stretching of the sphincters is based on a false premise. Unless the muscle is actually damaged, paralysis lasts less than thirty minutes in most cases, and in the process of recovering its contractile power the muscle contracts spasmodically, causing sudden violent pain. I have for some years utilized the principles of Bnie's<sup>28</sup> "average type" and "amputative type" methods of hemorrhoidectomy which may be adapted to the particular condition in each particular patient for suitable plastic procedure.

*Injection Treatment of Hemorrhoids.*—This method of treatment, originated in 1866 by Blackwood,<sup>7</sup> exploited by charlatans and ignorant practitioners, was for many years in disrepute because of the many unfortunate complications incurred. Today, with proper recognition of its limitations, it is a frequently used and valuable method of treatment in selected cases. It is almost universally conceded and emphasized that injection therapy is restricted to the treatment of internal hemorrhoids and should never be used for external hemorrhoids. Injection of a sclerosing solution below the mucocutaneous line produces severe pain and is usually followed by extensive painful necrosis and sloughing of tissue. Perhaps not sufficient stress has been laid upon its contraindications in the treatment of internal hemorrhoids complicated by inflammation, thrombosis, marked ulceration, or strangulation, or in the presence of associated pathologic conditions, such as cryptitis, fissure, or fistula. This method is ideally suited to the treatment of uncomplicated, superficially eroded internal hemorrhoids in the patient whose only symptom is bleeding. It may be employed for some measure of palliative relief in patients with large combined externointernal hemorrhoids who are unable for one reason or another to undergo hemorrhoidectomy. Any patient who has pain as a primary complaint must of necessity have some pathologic condition at or below the level of the mucocutaneous line and will not be relieved of his pain by injection treatment. All too frequently this error is made. Although the majority of published reports claim permanent cure in better than 85 per cent of cases, there are many proctologists today who sincerely believe that this form of treatment exceptionally produces permanent cure. When treatment is advised

and undertaken, their patients are told that its effects may not be expected to be permanent, but that it will satisfactorily relieve their symptoms for a period of from one to five years and that further treatment may eventually be required. Some of this group believe that treatment should be continued only to the point of relief of symptoms, usually bleeding, rather than to attempt by repeated treatments to entirely eliminate all traces of internal hemorrhoids.

The technique of injection consists in depositing a sclerosing solution through the mucous membrane into the submucosa containing the hemorrhoidal veins. A chemical inflammatory reaction results with influx of leucocytes and the ultimate production of fibrous tissue which in its contraction compresses and obliterates the hemorrhoidal veins. It has been recommended that injection be done just at the upper limits of the internal hemorrhoid, thereby obliterating the superior hemorrhoidal veins above the varicosities, with the result that subsequently the remainder of the hemorrhoid will be smaller in size and more readily sclerosed. Also such high injection is suggested to fix the upper extent of the hemorrhoid so that when subsequent injection is done into the main mass of the hemorrhoid and temporary swelling occurs there will be no danger of prolapse and incarceration. The interval between treatments varies from five to fourteen days. Commonly, treatment is given once weekly, the same hemorrhoid not being injected oftener than every second week. The number of treatments given varies from one to fourteen, the average being six to eight. The amount of solution injected varies for different solutions used, but there also is a difference of opinion as to the relative amount of solution that should be injected. Some employ from a few minims to 1 c.c. Others distend the hemorrhoid until all folds are obliterated and the mucosa shows definite pallor. Ordinarily pallor of the mucous membrane is an indication that the injection is being made too superficially and necrosis is liable to ensue if injection is continued. Competent treatment by injection necessitates thorough knowledge of the anatomy of the anorectum and a certain adeptness in the development of proper exposure with a suitable instrument.

It is impossible to estimate in what percentage of patients injection treatment is to be recommended. Essentially all proctologists employ this method in at least some patients. The number of patients who are given palliative treatment by this means in order to avoid loss of time and avoidance of expense swells the proportion who are so treated probably to about 50 per cent. It is only the rare misguided enthusiast who has abandoned operative treatment entirely for injection therapy.<sup>19</sup> In general the extensive enthusiasm of a decade ago has been tempered by experience and this method of treatment is now being given its more proper position of importance in the treatment of hemorrhoids.

*Sclerosing Solutions.*—The ideal reagent for injection treatment is one which will produce sufficient irritation and reaction to result in adequate fibrosis without actually producing necrosis. Absence of toxicity and idiosyncrasy is desirable. Many agents have been used, including 70 per cent alcohol,<sup>20</sup> epinephrine, hydrochloric acid, ferric chloride, 50 per cent glucose,<sup>123, 124</sup> hypertonic sodium chloride, horse serum, salicylic acid, trinitrophenol, quinine 30 per cent solution,<sup>19</sup> quinine and urethane, quinine and urea dichlorhydrolactate, sodium morrhuate and zinc chloride. At the present time, however, there are only two reagents widely used for the purpose, quinine and urea hydrochloride and phenol in vegetable oil.

Quinine and urea hydrochloride (5 per cent) was originally suggested by Terrell<sup>181</sup> and has been found very satisfactory by many.<sup>9, 11, 12, 28, 37, 97, 103, 156, 163, 168</sup> As a rule from 0.5 to 1 c.c. is injected into each hemorrhoid. Although idiosyncrasy is rare, a careful history should be ascertained before treatment. Sloughing occurs only as the result of faulty technique due to such errors as too superficial injection, injection too close to the mucocutaneous line, injecting too much solution or a second injection into the same hemorrhoid after too short an interval of time.

Phenol has long been a popular reagent for injection of internal hemorrhoids. When originally used in as high as 20 per cent and 30 per cent solutions, necrosis and sloughing occurred in a fairly high percentage of cases, so that a certain prejudice remains today to its use. However, 5 per cent phenol in vegetable oil has been found to produce about the same degree of reaction as 5 per cent quinine and urea hydrochloride<sup>7</sup> and is used by a considerable number of proctologists.<sup>43, 166, 189, 195</sup> Formerly glycerin was used as a vehicle for phenol, but chemical stricture from the continued reaction to the unabsorbed glycerin has been reported.<sup>153</sup> It has been found that this objection is corrected by the use of vegetable oil in place of glycerin. Five per cent phenol in vegetable oil is being used in amounts of from 1 to 10 c.c. injected into a single hemorrhoid by the same technique as that used for quinine and urea hydrochloride. The amount to be injected may be determined by the degree of redundancy of the mucous membrane that is present.<sup>43</sup> As with quinine and urea hydrochloride, sloughing should not occur if proper technique is employed.

*Electrical Treatment of Hemorrhoids.*—Occasional reports are found in the literature extolling the advantages of positive or negative galvanism, "coagulation" by bipolar diathermy, or "desiccation" by monopolar high frequency current.<sup>3, 17, 21, 61, 65, 68, 80, 116, 162, 184</sup> This subject can be adequately covered by two quotations:

1. Buie:<sup>28</sup> "The so-called coagulating needle has been in use for several decades and is widely used by those who claim to have certain



secret methods which are painless and which 'dissolve' the hemorrhoid instead of cutting it out."

2. Kleckner:<sup>105</sup> "This method . . . requires expensive equipment and thorough training to accomplish in a round-about way what can be done more easily, more quickly and equally as well by such certain methods as injection and operation."

#### PROLAPSE

*Classification.*—For many years protrusion of the rectal mucosa through the anus has been called incomplete or partial prolapse and invagination of all the coats of the rectal wall has been called complete prolapse. The latter has been subdivided into three types: first degree (external displacement of the lower rectal wall with complete eversion of the anal canal), second degree (external displacement of the lower rectal wall without disturbance of the wall of the anal canal), and third degree (invagination of the upper rectal or sigmoid wall into the rectal ampulla without external displacement). Martin<sup>119</sup> in 1932 argued that this classification should be reversed. Buie<sup>28</sup> divides the classification into two chief headings. "Visible prolapse" is subdivided into the partial type (incomplete prolapse) and the complete type, first degree and second degree (comparable in old classification). "Concealed rectal prolapse" is comparable to third degree complete prolapse in the old classification. Bacon,<sup>8</sup> following Martin,<sup>118</sup> proposes a change in nomenclature, using the term "prolapse" to apply only to the incomplete or partial type and utilizing the term "proci-dentia" for abnormal descent of all coats of the rectum.

*Treatment.*—The many operative procedures that have been advocated for the treatment of rectal prolapse are mute evidence of the fact that such procedures are all too often followed by disappointment and recurrence. The principle methods of rectorrhaphy, rectopexy, colopexy, and amputative resection are well described by Bacon.<sup>7</sup> Buie<sup>28</sup> describes an amputative resection which he believes, properly performed, will correct far more of these conditions than have been previously accredited to it, even to the most extensive prolapse. C. W. Mayo<sup>120</sup> recently described a new intra-abdominal technique in which multiple fascial strips are utilized for obliteration and fixation of the median perineal hernia. He considers this an important correction of a major weakness in the classical operation of Moseowitz.<sup>121</sup> Murr-rieta<sup>122</sup> has reported recently a unique operation applicable to all forms and degrees of prolapse and proci-dentia based upon his technique of valvotomy.<sup>123</sup> The use of the elastic ligature method of amputation has been largely discontinued although articles recommending its use in selected cases have appeared by Reid, Wangenstein, and Eliason.

Great advances in the treatment of prolapse have been made by the use of injections of sclerosing solutions to produce fibrosis and support. This method has been found to be almost uniformly successful in all degrees of incomplete prolapse and frequently has been efficacious in the correction of variable degrees of complete prolapse. Many now believe that all degrees of prolapse should be treated by injection and only if failure results should operation be considered. Smith<sup>165</sup> has not found it necessary to do a surgical operation, other than the injection of hydrochloric acid, in ten years. Hanes<sup>74</sup> claims that he has never failed to cure a patient who didn't have straining. Both submucosa and perirectal injection may be utilized.

*Hydrochloric Acid.*—Hanes<sup>75, 76</sup> injects 50 to 60 c.c. of 1:3,000 hydrochloric acid into the perirectal tissues, preceded by a similar amount of 0.5 per cent novocaine. Smith<sup>166</sup> uses a dilution of 1:1,500. I have obtained very satisfactory results by the use of the latter dilution in amounts up to 240 c.c. injected with the patient under spinal anesthesia without local novocaine infiltration.

*Quinine and Urea Hydrochloride.*—Terrell<sup>179</sup> has for fifteen years used this solution with invariable success in children, injecting 0.5 c.c. of 2 to 3 per cent solution in 2, 3, or 4 quadrants into the submucosa just above the anorectal line. Only a few cases require more than one treatment. Buie<sup>28</sup> uses this solution in 5 per cent strength, injecting 2 to 3 c.c. into the submucosa in 2 to 3 different places and repeating the treatment in several days. He has used the same solution for perirectal injection in mild cases of complete prolapse.

*Phenol in Vegetable Oil.*—This solution in 5 per cent strength has been advocated by Gabriel,<sup>56</sup> who makes a series of high submucosal injections, 2 c.c. in each of six to eight different sites. In combination with this he injects perirectally, posteriorly and on either side, 3 c.c. of Swinford Edwards solution (quinine sulfate gr. 12; dilute sulfuric acid, minims 30; and distilled water, minims 30, sterilized by boiling). The Gabriel technique has been followed and praised by others.<sup>23, 42, 132</sup> Alcohol, 70 to 95 per cent, has been advocated by many.<sup>40, 51, 58, 127, 135, 144</sup>

(To be continued in the July issue. The references will accompany the second section.)

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for many years. Functional localization and clinical interpretations are brought into line with this morphologic concept.

The midbrain and diencephalon naturally follow in this order. The various nuclei in the thalamic regions are admirably summarized as to location, structure, and function.

After some general considerations on development and lobulation of the cerebral hemispheres, basal ganglia and general organization of the white matter, brain ventricles, choroid plexus and cerebrospinal fluid, the visual system (including the eyeball) is satisfactorily covered with the usual ontogenetic introduction. The olfactory apparatus is similarly treated.

The final chapters deal with the structure of the cerebral cortex (cytoarchitecture of the better known regions), the efferent system as a unit (the pyramidal, extrapyramidal and corticopontocerebellar paths) and the function of the thalamus and cerebral localization. These topics are strictly modern.

The entire book is well planned. The language is clear and uninvolved. The nomenclature is simple. It is not an anatomic atlas but rather a functional analysis of the nervous system. There is nothing on the blood supply. Much space is spared by reducing controversial topics to a minimum. A surprising amount of neurology has been condensed into twenty-four short chapters, each of which contains a selected list of references. There is a twenty-five-page index, and there are 232 figures. Needless to say, the workmanship and material are of high quality.

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**Life and Letters of Fielding H. Garrison.** By Solomon R. Kagan. Cloth. Pp. 287, with 3 illustrations. Boston, 1938. The Medico-Historical Press. \$3.

This, the first of the biographies of America's greatest medical historian, probably will not be the last. Kagan's treatise is written in two parts. The one contains an interesting collection (selected) of Garrison's letters which reveal the warmth of his friendship for his few intimate friends and the many-sided nature of his personality. The biographical sketch of Part I is a somewhat disjointed account written under the following captions: (1) General Survey of Garrison's Life, (2) Medical Historian and Medical Bibliographer, (3) Medical Biography, (4) The Teacher, (5) Love of Music, (6) The Man, and (7) Tributes.

The volume includes a complete chronological list of Garrison's published books and articles and concludes with an appendix of varied material.

Garrison gained the admiration of his peers for his lasting achievement in the writing of a great one-volume work on medical history, which its author described under the modest title of *An Introduction to the Study of Medical History*. It will be a long time probably before this readable volume crammed with solid information unearthed by its scholarly author through years of serious and patient study will be set aside because of the advent of a superior text.

Garrison exhibited in his *Medical History* an extraordinary capacity for coordinating facts and incidents—an ability which has not fallen upon his first biographer in the same liberal measure. There is, however, much to be said for the monograph and everyone who admired Garrison and his work will want to possess this volume and gain a more intimate acquaintance with this shy and modest but talented genius. Identified as he was over a period of years with the Army Medical Library and its interests and activities, it is somewhat disconcerting to learn that he never enjoyed other than temporarily the position of Librarian of the Army Medical Library.

## Book Reviews

Textbook of Neuroanatomy and the Sense Organs. By O. Larsell, Professor of Anatomy, University of Oregon Medical School. Pp. 343, with 232 illustrations. New York, London, 1939. D. Appleton-Century Company. \$6.

This meritorious book has been written primarily for first-year medical students, but it will be found extremely useful to all who wish a clear, concise treatise on the nervous system from the functional point of view.

After a brief consideration of the phylogenetic emergence of the synaptic nervous system, establishment of the reflex arc, embryology, and histogenesis, there follows a terse description of the structure and the functional components of the peripheral nerves with clinical interpretation of some of the commoner lesions of spinal nerves. Sensory and motor endings are satisfactorily covered and well illustrated.

In the chapter on the spinal cord and its meninges, the fiber tracts are effectively treated by colored cross sections and black-and-white diagrams of the general course and connections to higher levels. One may question the relative size of some of the tracts. Chordotomy indicates that a larger area is occupied by the lateral spinothalamic tract than is allotted, particularly in the cervical cord, while the anterior (ventral) spinocerebellar tract is oversized. Technically it would seem better to place the anterior corticospinal (direct pyramidal) tract nearest the ventral median fissure throughout the cervical and upper thoracic levels instead of lateral to the sulcomarginal tract as is done here and in most texts. The ventral corticospinal tract regularly extends to the medial margin of the ventral funiculus. Clinical applications are mentioned at many points. On page 80 it is stated that in destruction of the anterior white commissure, as in syringomyelia, there is loss of pain and temperature sensations on the *opposite* side of the body, whereas the sensory loss is usually bilateral.

The approach to the brain is through the cranial nerves, which are analyzed in a masterly fashion. The description of the medulla oblongata is clarified by means of many excellent drawings. Figs. 94, 96, and 99 are not quite typical of the human brain stem with respect to the position of the tectospinal tract, which is too far dorsal and hence unduly reduces the size of the medial longitudinal bundle. Again the anterior spinocerebellar tract has been overemphasized at the expense of the lateral spinothalamic fasciculus whose clinical significance is of greater importance.

The visceral efferent and gustatory systems are briefly but accurately presented. The vestibular and auditory systems are introduced by a review of the embryology and histology of the inner ear. Well-planned cuts show the main fiber connections. A minor omission is noted in Fig. 134 where no direct descending vestibulo-spinal fibers in the medial longitudinal bundle are shown, although they have been clearly established by several relatively recent studies.

The cerebellum is considered under the author's new concept that it is composed of two main divisions; namely, flocculonodular lobe (vestibular in function) and corpus cerebelli (general proprioceptive). The corpus cerebelli is further divided into anterior and posterior lobes. The diagrams showing the fiber connections are very complete and undoubtedly represent the most trustworthy in existence, since the cerebellum has been the author's primary field of investigation.

the charging lion travels at the rate of a mile a minute, something that no conservative naturalist will substantiate. There is also so much neglect of accepted scientific fact that one's credulity is further strained. For instance, no such vein as the "celiac" is listed in Gray's *Anatomy*. Physiologists who have had experience with denervating the adrenal in the dog and cat know that all its nerve fibers do not come through the celiac ganglion, as many accessory ones reach it from the upper portion of the lumbar sympathetic chain. While this point has not been definitely settled in man, the assumption that celiac ganglionectomy results in complete denervation of the adrenal is not justified. Furthermore, granted that the celiac ganglia contain the nerve cells of all the postganglionic fibers to the upper abdominal viscera, their destruction must be followed by such an increased sensitivity to adrenaline and sympathin that vasoconstriction of the vascular bed cannot be greatly reduced.

The operation which Crile advocates to lessen the drive on the cardiovascular system consists of excision of the celiac ganglia and denervation of the aorta and adrenal glands. This complex network of ganglia and delicate nerve fibers is identified by palpation with the hand inserted to the wrist in the retroperitoneal space under the twelfth rib. By "touch anatomy" the operator must identify the major splanchnic nerve as it emerges from the crus of the diaphragm, the adrenal gland, as well as the surrounding arteries and veins. The celiac ganglion must then be freed up and its branches cut away from the surrounding vessels by a long scissors inserted along the tip of the index finger. The major splanchnic nerve "is the only leading string to the most important unit in this anatomical jungle." The surgeon must differentiate fine nerve strands from small veins and particularly avoid injury to the blood supply of the adrenal or deep hemorrhage. While such a dissection is possible for the author, who has denervated countless adrenals for neurocirculatory asthenia, hyperthyroidism, peptic ulcer and Raynaud's disease, one must protest against its adoption by the ordinary surgeon. Even if the operator avoids the complications mentioned above, it must be borne in mind that it is an established physiologic fact that any sympathetic fibers which are left behind can maintain the original tone of the partly denervated structures. Inasmuch as at least two satisfactory approaches have been used to expose this entire area to direct visual dissection, why should it ever be attempted without the help of the eyes?

An examination of the follow-up statistics presented will fail to convince the critical clinician that the patients who have been submitted to celiac ganglionectomy have achieved as significant a reduction in blood pressure as has been observed in other clinics after intrathoracic excision of the splanchnic nerves, or after a subdiaphragmatic resection which includes the upper portion of the lumbar sympathetic trunks as well as the structures removed by Crile. Figures given in Table 9 show an average reduction in 85 cases from 217/133 to 169/110 before discharge from the hospital. One year postoperatively 16 patients are recorded as having pressures averaging 196/121. There was striking improvement in the subjective symptoms of many of these patients, but this has followed other operations for this condition. Very little excuse can be seen for advocating an incomplete method of surgical denervation by a blind approach, when far better operative exposures of these structures are in use in other clinics.

The whole status of sympathectomy in the treatment of hypertension is still definitely on trial. Surgeons have received little encouragement from animal investigation and the leading medical authorities who have studied the disease are still not convinced that real benefit follows sympathectomy. A careful perusal of this book has not convinced the reviewer that it has advanced our understanding of essential hypertension.

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**Diseases of the Thyroid, Parathyroid and Thymus.** By Andre Crotti, M.D., formerly First Assistant of the Pathological Laboratory at University of Lausanne, Switzerland. Cloth. Ed. 3. Pp. 1229, with 262 illustrations and 39 plates in color. Philadelphia, 1938, Lea & Febiger. \$20.

This encyclopedic volume contains 51 chapters and more than 50 pages of bibliography. It is essentially a clinical treatise dealing with the problems of the thyroid, parathyroids, and thymus.

The author believes in the infectious origin of goiter, although he concedes an important role to iodine. If local environment or other factors did not play a part in the pathogenesis of goiter, in other words, if goiter were a pure deficiency disease, it should be largely the same, the world over, which, of course, it is not. The author cites some experimental evidence, not very convincing, adduced by himself which purports to give the infection factor greater credence.

The author believes that the presence of a goiter sensitizes a patient to iodine. He believes also in so-called "iodin Basedow" described by Rilliet, Breuer, and Kocher, a thesis which this reviewer believes is still demanding of proof. The author does not believe that factual data warrant drawing a sharp distinction between exophthalmic goiter and adenomatous goiter with hyperthyroidism, an attitude which the reviewer shares. The author speaks of hyperthyroidism as a "thyro-neuro-polyglandular disease."

Crotti's book constitutes a valuable source book containing a great mass of factual data interspersed between which lie many impressionistic ideas of the author; whether the latter add to the value of the volume or detract from its worth, it must be conceded, is a debatable issue.

**The Surgical Treatment of Hypertension.** By George Crile. Pp. 239, with 52 illustrations. Philadelphia, 1938, W. B. Saunders Company. \$4.

The monograph, *The Surgical Treatment of Hypertension* by Dr. George Crile, describes the personal point of view of its author on the etiology of essential hypertension and its attack by resection of the celiac ganglia. Crile has formulated the theory that since energy output of the organism is controlled by the brain, thyroid, and sympathoadrenal system, and since this triad is most highly developed in the lion and in man, the cardiovascular systems of these species are subjected to the greatest strain. His report that the large cats develop arteriosclerosis when kept in captivity is of great interest. Whereas the lion, once his belly is filled, lies down to sleep, man is in a perpetual state of activity. The sequel to this constant drive is the induction of scarring in the arterial tree and the development of hypertension. In further support of this hypothesis Crile states that the disease is due to an inherited large size of the celiac ganglia and the associated nerve structures which he has observed at operation. As listed by the author, the most important links in this system of energy control are the adrenal medulla and the celiac and aortic plexuses. Little mention is made of all the recent work on the autonomic pressor centers in the premotor cortex and diencephalon, but the medulla of the adrenal gland is considered as the "brain" of the sympathetic system and the genesis of human hypertension ascribed to "a pathologic physiology" of the celiac, aortic, and adrenal nerve plexuses. Few clinicians will subscribe to the author's statement that "hyperthyroidism, neuro-circulatory asthenia, and Raynaud's disease are abated or cured by adrenal denervation or celiac ganglionectomy."

The ideas above are stimulating and provocative to a new line of thought, but as one reads the book through one finds numerous exaggerations, such as that

the charging lion travels at the rate of a mile a minute, something that no conservative naturalist will substantiate. There is also so much neglect of accepted scientific fact that one's credulity is further strained. For instance, no such vein as the "celiac" is listed in Gray's *Anatomy*. Physiologists who have had experience with denervating the adrenal in the dog and cat know that all its nerve fibers do not come through the celiac ganglion, as many accessory ones reach it from the upper portion of the lumbar sympathetic chain. While this point has not been definitely settled in man, the assumption that celiac ganglionectomy results in complete denervation of the adrenal is not justified. Furthermore, granted that the celiac ganglia contain the nerve cells of all the postganglionic fibers to the upper abdominal viscera, their destruction must be followed by such an increased sensitivity to adrenaline and sympathin that vasoconstriction of the vascular bed cannot be greatly reduced.

The operation which Crile advocates to lessen the drive on the cardiovascular system consists of excision of the celiac ganglia and denervation of the aorta and adrenal glands. This complex network of ganglia and delicate nerve fibers is identified by palpation with the hand inserted to the wrist in the retroperitoneal space under the twelfth rib. By "touch anatomy" the operator must identify the major splanchnic nerve as it emerges from the crus of the diaphragm, the adrenal gland, as well as the surrounding arteries and veins. The celiac ganglion must then be freed up and its branches cut away from the surrounding vessels by a long scissors inserted along the tip of the index finger. The major splanchnic nerve "is the only leading string to the most important unit in this anatomical jungle." The surgeon must differentiate fine nerve strands from small veins and particularly avoid injury to the blood supply of the adrenal or deep hemorrhage. While such a dissection is possible for the author, who has denervated countless adrenals for neurocirculatory asthenia, hyperthyroidism, peptic ulcer and Raynaud's disease, one must protest against its adoption by the ordinary surgeon. Even if the operator avoids the complications mentioned above, it must be borne in mind that it is an established physiologic fact that any sympathetic fibers which are left behind can maintain the original tone of the partly denervated structures. Inasmuch as at least two satisfactory approaches have been used to expose this entire area to direct visual dissection, why should it ever be attempted without the help of the eyes?

An examination of the follow-up statistics presented will fail to convince the critical clinician that the patients who have been submitted to celiac ganglionectomy have achieved as significant a reduction in blood pressure as has been observed in other clinics after intrathoracic excision of the splanchnic nerves, or after a subdiaphragmatic resection which includes the upper portion of the lumbar sympathetic trunks as well as the structures removed by Crile. Figures given in Table 9 show an average reduction in 85 cases from 217/133 to 169/110 before discharge from the hospital. One year postoperatively 16 patients are recorded as having pressures averaging 196/121. There was striking improvement in the subjective symptoms of many of these patients, but this has followed other operations for this condition. Very little excuse can be seen for advocating an incomplete method of surgical denervation by a blind approach, when far better operative exposures of these structures are in use in other clinics.

The whole status of sympathectomy in the treatment of hypertension is still definitely on trial. Surgeons have received little encouragement from animal investigation and the leading medical authorities who have studied the disease are still not convinced that real benefit follows sympathectomy. A careful perusal of this book has not convinced the reviewer that it has advanced our understanding of essential hypertension.

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*Medicine in Modern Society.* By David Riesman. Cloth. Pp. 226. Princeton, N. J., 1938, Princeton University Press. \$2.50.

The author of this book is a widely known, admired, and beloved clinician, teacher, scholar, and investigator. Dr. Riesman's many papers in the fields of pathology, medicine, and medical history have been so greatly appreciated by medical readers that they welcome enthusiastically the announcement of this new semi-historical, semi-philosophical book from his pen.

*Medicine in Modern Society* was written for the general rather than for the medical reader; but physicians will find that familiar facts are here presented in a new and interesting setting and that the controversial subject of the dispensation of medical care is discussed frankly and realistically.

The basis of this book was a series of Princeton University lectures, the Vnuxem Lectures, in the development of which the author was guided by his belief that "the history of medicine is in reality an epitome of the history of civilization and should form a part of every man's culture."

In a simple, fascinating manner Dr. Riesman paints a picture of the high points in the development of the science and the art of medicine. Hippocrates, Galen, Vesalius—"the Columbus of anatomy"—Harvey, Jenner, McDowell, Long, Morton, Simpson, Semmelweis, Holmes, Lister, Pasteur, Koch and others down to the present day all take their places briefly but impressively in the pageant of medical history which passes before the reader in a few brief pages.

Opium, mercury, cinchona, digitalis, vaccination, anesthesia, antiseptics, anti-toxins, x-ray, radium, salvarsan, insulin, liver therapy, allergy, endocrinology, psychoanalysis, hormones, vitamins, viruses, and even fever therapy and sulfanilamide are briefly and deftly fitted into the picture. Many well-chosen anecdotes and personal experiences add interest to the story.

The methods and the problems involved in arriving at a diagnosis and in deciding upon a course of treatment are presented in a way that should make for better understanding between patient and doctor. In discussing the importance of an accurate history of the patient's illness and the delight that some patients seem to take in refusing to answer the physician's questions truthfully or completely, he recalls "a story told of the great Iron Chancellor. He had had many physicians, all of whom he discharged. Finally he summoned a Doctor Schweininger, who began to ask him many questions. Impatiently Bismarck said to the doctor, 'You should not ask so much—you should know what ails me without questioning.' 'Your Highness,' answered the doctor, 'I would suggest you call a veterinarian; he asks no questions.'"

The present status of medicine and medical education is described as exemplifying the best of our civilization. Medical cults and superstitions are explained. The roles of the specialist and the family physician of the future are set forth so clearly and so sanely that everyone can understand.

The chapter on the social outlook of medicine is a thoughtful, realistic, and sane consideration of the social problems today which the medical profession is confronted with. That certain problems exist Dr. Riesman admits, but he concludes that "a profession that has elevated the standards of medical education to a level unequalled in the civilized world, has regulated hospitals until today no nation can match ours, publishes the best medical journal in existence together with many other works that serve to educate the American physician; brings together annually thousands of doctors from all over the land for a week of intensive postgraduate study which is a model for the world—such an Association can I think be trusted to collaborate with socially minded laymen toward a plan for distributing medical care, both curative and preventive, to all people." On the other hand, he says, this Association "must take the lead in the inevitable movement of reform. If it fails to lead, then it will be obliged to follow those who have neither the knowledge, the wisdom, nor the incentive to preserve what is best in American medicine."

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